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SEARCH REQUEST FORM

Scientific and Technical Information Center:

Requester's Full Name: Jeffrey E. Russell Examiner #: 62785 Date: 2-14-2003
 Art Unit: 1654 Phone Number 308 3975 Serial Number: 01/873,899
 Mail Box and Bldg/Room Location: _____ Results Format Preferred (circle): PAPER DISK E-MAIL
CM-1 11B13/CM-1 9807

If more than one search is submitted, please prioritize searches in order of need.

 Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

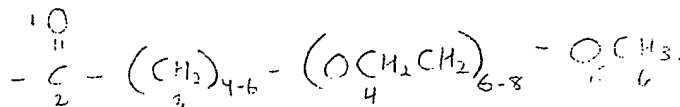
Title of Invention: Methods of Insulin Drug-Oligonucleotide Conjugates Comprising Polynucleotide Sequences

Inventors (please provide full names): N. L. Worthing, C. Price, A. Anton, B. Radhakrishnan,
A. Openbaugh

Earliest Priority Filing Date: 6-4-2001

For Sequence Searches Only Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

Please search the following partial structure:



If necessary, please use the keywords conjugate, insulin.

Thank you.

Mary Jane Ruhl
 Tech. Info. Specialist, STIC
 TC-1600
 CM-1, Room 6A-06
 Phone: 605-1155

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	Type of Search	Vendors and cost where applicable
Searcher: _____	NA Sequence (#) _____	STN _____
Searcher Phone #: _____	AA Sequence (#) _____	Dialog _____
Searcher Location: _____	Structure (#) _____	Questel/Orbit _____
Date Searcher Picked Up: _____	Bibliographic _____	Dr. Link _____
Date Completed: <u>2/20/03</u>	Litigation _____	Lexis/Nexis _____
Searcher Prep & Review Time: _____	Fulltext _____	Sequence Systems _____
Clerical Prep Time: _____	Patent Family _____	WWW/Internet _____
Online Time: _____	Other _____	Other (specify) _____

4 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

5 REFERENCES IN FILE CAPLUS (1962 TO DATE)

- REFERENCE 1: 138:29120 Preparation of peptide drug-alkylene glycol oligomer conjugates. Ekwuribe, Nnochiri N.; Price, Christopher H.; Ansari, Aslam M.; Odenbaugh, Amy L. (Nobex Corporation, USA). PCT Int. Appl. WO 2002098446 A1 20021212, 201 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US17567 20020604. PRIORITY: US 2001-873797 20010604.
- AB A non-polydispersed mixt. of conjugates in which each conjugate in the mixt. comprises a peptide drug coupled to an oligomer that includes a polyalkylene glycol moiety is disclosed. The mixt. may exhibit higher in vivo activity than a polydispersed mixt. of similar conjugates. The mixt. may be more effective at surviving an in vitro model of intestinal digestion than polydispersed mixts. of similar conjugates. The mixt. may result in less inter-subject variability than polydispersed mixts. of similar conjugates. Thus, non-polydispersed hexaethylene glycol was treated with phosgene soln., followed by treatment with N-hydroxysuccinimide (NHS) to give the NHS ester. Human growth hormone (Saizen) was allowed to react with the NHS ester to give the conjugate.
- REFERENCE 2: 138:25334 Methods of preparing monodispersed mixtures of polymers having polyethylene glycol moieties. Ekwuribe, Nnochiri N.; Price, Christopher H.; Ansari, Aslam M.; Odenbaugh, Amy L. (Nobex Corporation, USA). PCT Int. Appl. WO 2002098949 A1 20021212, 35 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US17619 20020604. PRIORITY: US 2001-873731 20010604.
- AB The method comprises reacting monodispersed mixts. of compds. R1(OC2H4)nO-X+ (R1 = H, lipophilic moiety; n = 1-25; and X+ = pos. ion) with monodispersed mixts. of compds. R2(OC2H4)mOMs (R2 = H, lipophilic moiety; m = 1-25; Ms = CH3SO2-) under conditions sufficient to form monodispersed mixts. of polymers comprising polyethylene glycol moieties R2(OC2H4)m+nOR1. The method reduces the no. of steps and/or overall synthesis time and utilizes milder reaction conditions than those used in conventional methods. Thus, 27.3 parts hexaethylene glycol monobenzyl ether was mixed with 3.225 parts sodium hydride n anhyd. toluene at 0.degree. for 30 min and at room temp. for 5 h and reacted with 19.21 parts Et 6-methylsulfonyloxyhexanoate (obtained from Et 6-hydroxyhexanoate and methanesulfonyl chloride) to form 16.22 parts 6-{2-[2-(2-{2-[2-(2-benzyloxyethoxy)ethoxy]ethoxy}ethoxy)ethoxy]hexanoic acid Et ester.
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AB A mixt. of conjugates in which each conjugate in the mixt. comprises a growth hormone drug coupled to an oligomer that includes a polyalkylene glycol moiety is disclosed. Thus, non-polydispersed hexaethylene glycol was treated with phosgene soln., followed by treatment with N-hydroxysuccinimide (NHS) to give the NHS ester. Human growth hormone (Saizen) was dissolved in DMSO and allowed to react with the NHS ester to give the conjugate.

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AB A mixt. of conjugates in which each conjugate in the mixt. comprises a calcitonin drug coupled to an oligomer that includes a polyalkylene glycol moiety is disclosed. The mixt. may lower serum calcium levels in a subject by 10, 15 or .gtoreq.20%. Moreover, the mixt. may be more effective at surviving an in vitro model of intestinal digestion than non-conjugated calcitonin. Furthermore, the mixt. may exhibit a higher bioavailability than the non-conjugated calcitonin. Thus, non-polydispersed hexaethylene glycol was treated with phosgene soln., followed by treatment with N-hydroxysuccinimide (NHS) to give the NHS ester. Salmon calcitonin was allowed to react with the NHS ester to give the conjugate.

REFERENCE 5: 138:16621 Preparation of insulin-alkylene glycol oligomer conjugates. Ekwuribe, Nnochiri N.; Price, Christopher H.; Ansari, Aslam M.; Odenbaugh, Amy L.; Radhakrishnan, Balasingam (Nobex Corporation, USA). PCT Int. Appl. WO 2002098232 A1 20021212, 127 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US17574 20020604. PRIORITY: US 2001-873899 20010604.

AB A mixt. of conjugates in which each conjugate in the mixt. comprises an insulin drug coupled to an oligomer that includes a polyalkylene glycol moiety is disclosed. The mixt. may exhibit higher in vivo activity than a polydispersed mixt. of similar conjugates. The mixt. may also be more effective at surviving an in vitro model of intestinal digestion than polydispersed mixts. of similar conjugates. The mixt. may also result in less inter-subject variability than polydispersed mixts. of similar conjugates. Thus, non-polydispersed hexaethylene glycol was treated with

phosgene soln., followed by treatment with N-hydroxysuccinimide (NHS) to give the NHS ester. Human insulin was dissolved in DMSO and allowed to react with the NHS ester to give the conjugate.

L3 ANSWER 2 OF 4 REGISTRY COPYRIGHT 2003 ACS
RN 477775-62-5 REGISTRY
CN 2,5,8,11,14,17,20,23,26-Nonaoxadotriacontan-32-oic acid (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C23 H46 O11
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

PAGE 1-A

MeO-CH₂-CH₂-O-CH₂-CH₂-O-CH₂-CH₂-O-CH₂-CH₂-O-CH₂-CH₂-O-

PAGE 1-B

-CH₂-CH₂-O-CH₂-CH₂-O-CH₂-CH₂-O-(CH₂)₅-CO₂H

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

5 REFERENCES IN FILE CA (1962 TO DATE)
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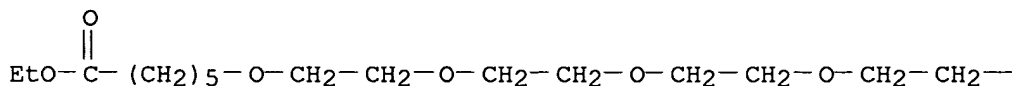
effective at surviving an in vitro model of intestinal digestion than non-conjugated calcitonin. Furthermore, the mixt. may exhibit a higher bioavailability than the non-conjugated calcitonin. Thus, non-polydispersed hexaethylene glycol was treated with phosgene soln., followed by treatment with N-hydroxysuccinimide (NHS) to give the NHS ester. Salmon calcitonin was allowed to react with the NHS ester to give the conjugate.

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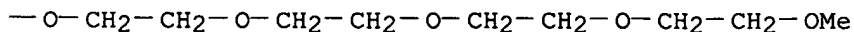
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L3 ANSWER 3 OF 4 REGISTRY COPYRIGHT 2003 ACS
RN 477775-61-4 REGISTRY
CN 2,5,8,11,14,17,20,23,26-Nonaoxadotriacontan-32-oic acid, ethyl ester (9CI)
(CA INDEX NAME)
FS 3D CONCORD
MF C25 H50 O11
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

PAGE 1-A



PAGE 1-B



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

5 REFERENCES IN FILE CA (1962 TO DATE)

5 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 138:29120 Preparation of peptide drug-alkylene glycol oligomer conjugates. Ekwuribe, Nnochiri N.; Price, Christopher H.; Ansari, Aslam M.; Odenbaugh, Amy L. (Nobex Corporation, USA). PCT Int. Appl. WO 2002098446 A1 20021212, 201 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US17567 20020604. PRIORITY: US 2001-873797 20010604.

AB A non-polydispersed mixt. of conjugates in which each conjugate in the mixt. comprises a peptide drug coupled to an oligomer that includes a polyalkylene glycol moiety is disclosed. The mixt. may exhibit higher in vivo activity than a polydispersed mixt. of similar conjugates. The mixt. may be more effective at surviving an in vitro model of intestinal digestion than polydispersed mixts. of similar conjugates. The mixt. may result in less inter-subject variability than polydispersed mixts. of similar conjugates. Thus, non-polydispersed hexaethylene glycol was treated with phosgene soln., followed by treatment with N-hydroxysuccinimide (NHS) to give the NHS ester. Human growth hormone (Saizen) was allowed to react with the NHS ester to give the conjugate.

REFERENCE 2: 138:25334 Methods of preparing monodispersed mixtures of polymers having polyethylene glycol moieties. Ekwuribe, Nnochiri N.; Price, Christopher H.; Ansari, Aslam M.; Odenbaugh, Amy L. (Nobex Corporation, USA). PCT Int. Appl. WO 2002098949 A1 20021212, 35 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US17619 20020604. PRIORITY: US 2001-873731 20010604.

AB The method comprises reacting monodispersed mixts. of compds. $R_1(OC_2H_4)_nO-X^+$ ($R_1 = H$, lipophilic moiety; $n = 1-25$; and $X^+ = \text{pos. ion}$) with monodispersed mixts. of compds. $R_2(OC_2H_4)_mOMs$ ($R_2 = H$, lipophilic moiety; $m = 1-25$; $Ms = CH_3SO_2-$) under conditions sufficient to form monodispersed mixts. of polymers comprising polyethylene glycol moieties $R_2(OC_2H_4)_m+nOR_1$. The method reduces the no. of steps and/or overall synthesis time and utilizes milder reaction conditions than those used in conventional methods. Thus, 27.3 parts hexaethylene glycol monobenzyl ether was mixed with 3.225 parts sodium hydride n anhyd. toluene at 0.degree. for 30 min and at room temp. for 5 h and reacted with 19.21 parts Et 6-methylsulfonyloxyhexanoate (obtained from Et 6-hydroxyhexanoate and methanesulfonyl chloride) to form 16.22 parts 6-{2-[2-(2-{2-(2-benzyloxyethoxy)ethoxy}ethoxy)ethoxy]ethoxy}hexanoic acid Et ester.

REFERENCE 3: 138:16637 Preparation of growth hormone drug-polyalkylene glycol oligomer conjugates. Ekwuribe, Nnochiri N.; Price, Christopher H.; Ansari, Aslam M.; Odenbaugh, Amy L. (Nobex Corporation, USA). PCT Int. Appl. WO 2002098452 A1 20021212, 145 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ,

DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US17504 20020604. PRIORITY: US 2001-873757 20010604.

AB A mixt. of conjugates in which each conjugate in the mixt. comprises a growth hormone drug coupled to an oligomer that includes a polyalkylene glycol moiety is disclosed. Thus, non-polydispersed hexaethylene glycol was treated with phosgene soln., followed by treatment with N-hydroxysuccinimide (NHS) to give the NHS ester. Human growth hormone (Saizen) was dissolved in DMSO and allowed to react with the NHS ester to give the conjugate.

REFERENCE 4: 138:16636 Preparation of calcitonin drug-alkylene glycol oligomer conjugates. Ekwuribe, Nnochiri N.; Price, Christopher H.; Ansari, Aslam M.; Odenbaugh, Amy L. (Nobex Corporation, USA). PCT Int. Appl. WO 2002098451 A1 20021212, 126 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US17575 20020604. PRIORITY: US 2001-873777 20010604.

AB A mixt. of conjugates in which each conjugate in the mixt. comprises a calcitonin drug coupled to an oligomer that includes a polyalkylene glycol moiety is disclosed. The mixt. may lower serum calcium levels in a subject by 10, 15 or .gtoreq.20%. Moreover, the mixt. may be more effective at surviving an in vitro model of intestinal digestion than non-conjugated calcitonin. Furthermore, the mixt. may exhibit a higher bioavailability than the non-conjugated calcitonin. Thus, non-polydispersed hexaethylene glycol was treated with phosgene soln., followed by treatment with N-hydroxysuccinimide (NHS) to give the NHS ester. Salmon calcitonin was allowed to react with the NHS ester to give the conjugate.

REFERENCE 5: 138:16621 Preparation of insulin-alkylene glycol oligomer conjugates. Ekwuribe, Nnochiri N.; Price, Christopher H.; Ansari, Aslam M.; Odenbaugh, Amy L.; Radhakrishnan, Balasingam (Nobex Corporation, USA). PCT Int. Appl. WO 2002098232 A1 20021212, 127 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US17574 20020604. PRIORITY: US 2001-873899 20010604.

AB A mixt. of conjugates in which each conjugate in the mixt. comprises an insulin drug coupled to an oligomer that includes a polyalkylene glycol moiety is disclosed. The mixt. may exhibit higher in vivo activity than a polydispersed mixt. of similar conjugates. The mixt. may also be more effective at surviving an in vitro model of intestinal digestion than polydispersed mixts. of similar conjugates. The mixt. may also result in less inter-subject variability than polydispersed mixts. of similar

conjugates. Thus, non-polydispersed hexaethylene glycol was treated with phosgene soln., followed by treatment with N-hydroxysuccinimide (NHS) to give give the NHS ester. Human insulin was dissolved in DMSO and allowed to react with the NHS ester to give the conjugate.

L3 ANSWER 4 OF 4 REGISTRY COPYRIGHT 2003 ACS
RN 405518-52-7 REGISTRY
CN 2,5,8,11,14,17,20-Heptaioxapentacosan-25-oic acid (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C18 H36 O9
SR CA
LC STN Files: CA, CAPLUS

PAGE 1-A

MeO-CH₂-CH₂-O-CH₂-CH₂-O-CH₂-CH₂-O-CH₂-CH₂-O-CH₂-CH₂-O-

PAGE 1-B

-CH₂-CH₂-O-(CH₂)₄-CO₂H

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 136:279111 Preparation of optionally substituted oxyethylene unit-containing alkanolic acid derivatives and their use in aerosol-delivered pharmaceuticals as suspension-stabilizing agents. Looker, Brian Edgar; Redgrave, Alison Judith; Lunniss, Christopher James; Reynolds, Derek Peter (Glaxo Group Limited, UK). PCT Int. Appl. WO 2002024623 A2 20020328, 27 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-GB4226 20010921. PRIORITY: GB 2000-23346 20000922; GB 2001-15438 20010623; GB 2001-16059 20010630.

AB The title acids or salts or solvates R₁[OCH(R₂)CH(R₃)]_mO(CH₂)_nCO₂H [n = 1-6; m = 1-15; R₁ = (CO)xCl-9alkyl or (CO)xCl-9fluoroalkyl (which fluoroalkyl moiety contains at least 1 fluorine atom and not more than 3 consecutive perfluorocarbon atoms); x = 0, 1; R₂, R₃ = Cl-3 alkyl, hydrogen; e.g., 2,5,8,11-tetraoxatridecan-13-oic acid] are prepd. and used in pharmaceutical aerosol formulations (e.g., salmeterol xinafoate formulation in HFA 134a contg. 10% of the title compds. relative to the drug) as aerosol suspension-stabilizing agents.

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L7 ANSWER 1 OF 5 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:946346 HCAPLUS

DOCUMENT NUMBER: 138:25334

TITLE: Methods of preparing monodispersed mixtures of polymers having polyethylene glycol moieties

INVENTOR(S): Ekwuribe, Nnochiri N.; Price, Christopher H.; Ansari, Aslam M.; Odenbaugh, Amy L.

PATENT ASSIGNEE(S): Nobex Corporation, USA

SOURCE: PCT Int. Appl., 35 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002098949	A1	20021212	WO 2002-US17619	20020604
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RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
US 2003004304	A1	20030102	US 2001-873731	20010604

PRIORITY APPLN. INFO.: US 2001-873731 A 20010604

AB The method comprises reacting monodispersed mixts. of compds.

R1(OC2H4)nO-X⁺ (R1 = H, lipophilic moiety; n = 1-25; and X⁺ = pos. ion) with monodispersed mixts. of compds. R2(OC2H4)mOMs (R2 = H, lipophilic moiety; m = 1-25; Ms = CH3SO2-) under conditions sufficient to form monodispersed mixts. of polymers comprising polyethylene glycol moieties R2(OC2H4)m+nOR1. The method reduces the no. of steps and/or overall synthesis time and utilizes milder reaction conditions than those used in conventional methods. Thus, 27.3 parts hexaethylene glycol monobenzyl ether was mixed with 3.225 parts sodium hydride n anhyd. toluene at 0.degree. for 30 min and at room temp. for 5 h and reacted with 19.21 parts Et 6-methylsulfonyloxyhexanoate (obtained from Et 6-hydroxyhexanoate and methanesulfonyl chloride) to form 16.22 parts 6-{2-[2-(2-[2-(2-benzyloxyethoxy)ethoxy]ethoxy)ethoxy]ethoxy}hexanoic acid Et ester.

IT 19278-10-5P, Diethylene glycol monomethyl ether, sodium salt

24342-68-5P 67025-23-4P 71182-98-4P

74654-05-0P 124668-93-5P 477775-57-8P

477775-58-9P 477775-59-0P 477775-60-3P

477775-61-4P 477775-62-5P 477849-81-3P

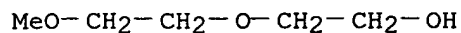
477849-86-8P

RL: IMF (Industrial manufacture); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; methods of prepg. monodispersed mixts. of polymers having polyethylene glycol moieties)

RN 19278-10-5 HCAPLUS

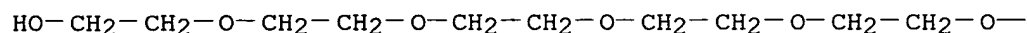
CN Ethanol, 2-(2-methoxyethoxy)-, sodium salt (8CI, 9CI) (CA INDEX NAME)



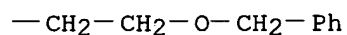
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RN 24342-68-5 HCAPLUS
CN 2,5,8,11,14,17-Hexaoxanonadecan-19-ol, 1-phenyl- (9CI) (CA INDEX NAME)

PAGE 1-A

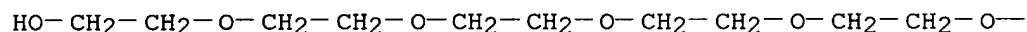


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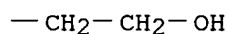
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CN 3,6,9,12,15-Pentaoxaheptadecane-1,17-diol, monosodium salt (9CI) (CA INDEX NAME)

PAGE 1-A

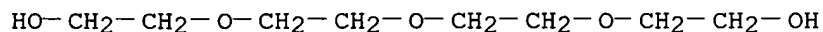


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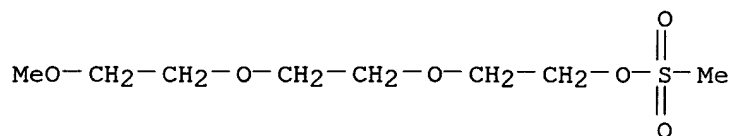
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CN Ethanol, 2,2'-[oxybis(2,1-ethanediylloxy)]bis-, monosodium salt (9CI) (CA INDEX NAME)



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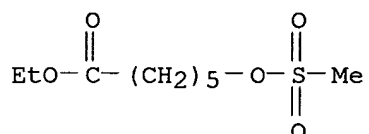
RN 74654-05-0 HCAPLUS
CN Ethanol, 2-[2-(2-methoxyethoxy)ethoxy]-, methanesulfonate (9CI) (CA INDEX NAME)

NAME)



RN 124668-93-5 HCAPLUS

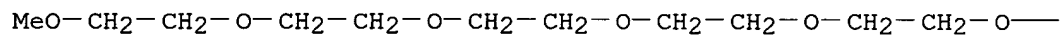
CN Hexanoic acid, 6-[(methylsulfonyl)oxy]-, ethyl ester (9CI) (CA INDEX NAME)



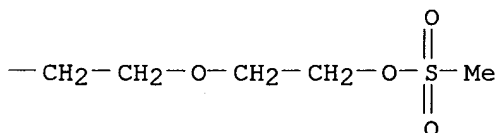
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CN 2,5,8,11,14,17,20-Heptaoxadocosan-22-ol, methanesulfonate (9CI) (CA INDEX NAME)

PAGE 1-A



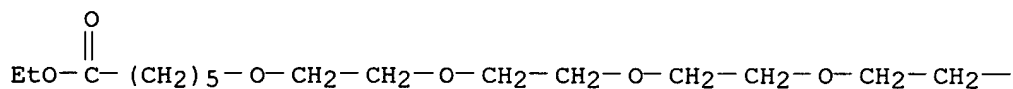
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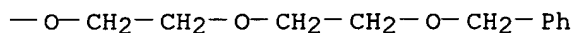
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PAGE 1-A

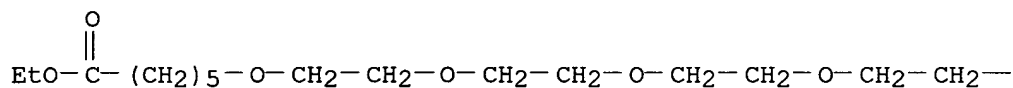


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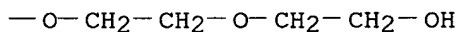


RN 477775-59-0 HCAPLUS
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(9CI) (CA INDEX NAME)

PAGE 1-A

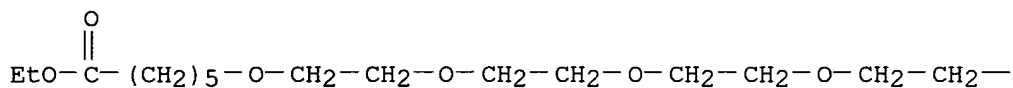


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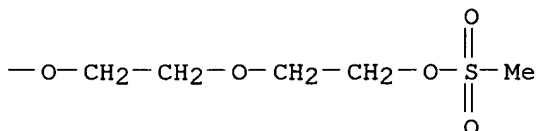


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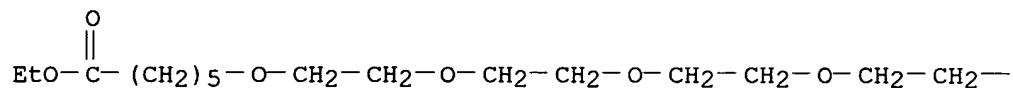


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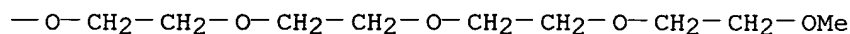


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(CA INDEX NAME)

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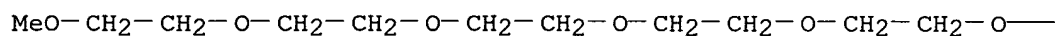


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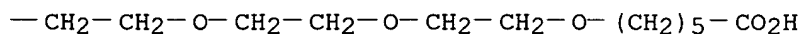


RN 477775-62-5 HCAPLUS
CN 2,5,8,11,14,17,20,23,26-Nonaoxadotriacontan-32-oic acid (9CI) (CA INDEX NAME)

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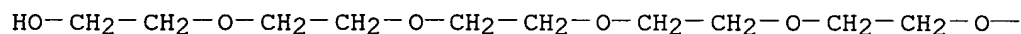


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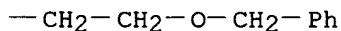
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PAGE 1-A

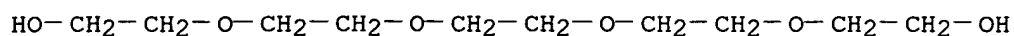


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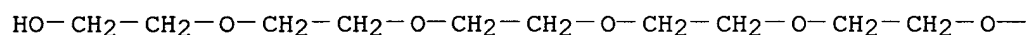
RN 477849-86-8 HCAPLUS
CN 3,6,9,12-Tetraoxatetradecane-1,14-diol, monosodium salt (9CI) (CA INDEX NAME)



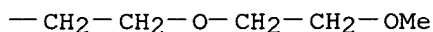
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IT 4437-01-8P, 2,5,8,11,14,17,20-Heptaoxidocosan-22-ol
 5702-16-9P 6048-68-6P 25322-68-3DP, derivs.
 25990-96-9P 27425-92-9P 114740-40-8P
 477775-63-6P
 RL: IMF (Industrial manufacture); PREP (Preparation)
 (methods of prepg. monodispersed mixts. of polymers having polyethylene
 glycol moieties)
 RN 4437-01-8 HCAPLUS
 CN 2,5,8,11,14,17,20-Heptaoxidocosan-22-ol (6CI, 8CI, 9CI) (CA INDEX NAME)

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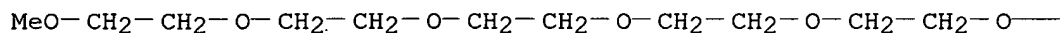


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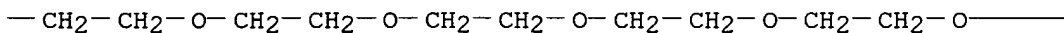


RN 5702-16-9 HCAPLUS
 CN 2,5,8,11,14,17,20,23,26,29,32,35-Dodecaoxaheptatriacontan-37-ol (8CI, 9CI)
 (CA INDEX NAME)

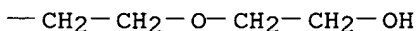
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PAGE 1-B

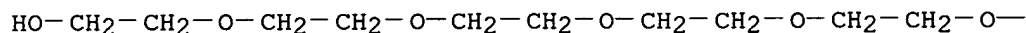


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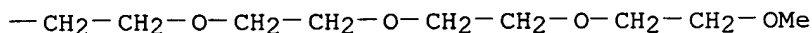


RN 6048-68-6 HCAPLUS
 CN 2,5,8,11,14,17,20,23,26-Nonaoxaoctacosan-28-ol (6CI, 8CI, 9CI) (CA INDEX
 NAME)

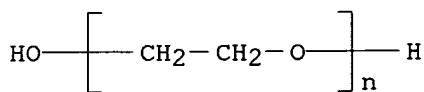
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PAGE 1-B

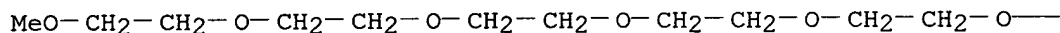


RN 25322-68-3 HCAPLUS
CN Poly(oxy-1,2-ethanediyl), .alpha.-hydro-.omega.-hydroxy- (9CI) (CA INDEX NAME)

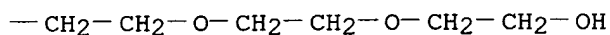


RN 25990-96-9 HCAPLUS
CN 2,5,8,11,14,17,20,23-Octaoxapentacosan-25-ol (6CI, 8CI, 9CI) (CA INDEX NAME)

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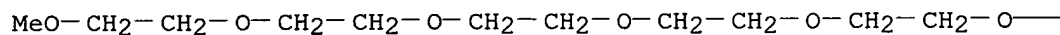


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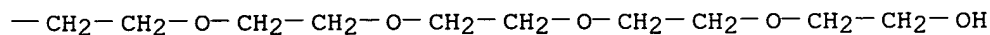


RN 27425-92-9 HCAPLUS
CN 2,5,8,11,14,17,20,23,26,29-Decaoxahentriacontan-31-ol (6CI, 8CI, 9CI) (CA INDEX NAME)

PAGE 1-A

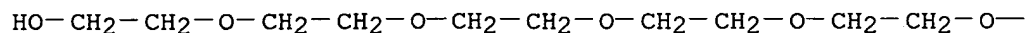


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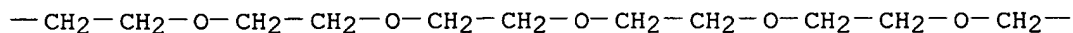


RN 114740-40-8 HCAPLUS
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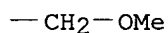
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PAGE 1-B



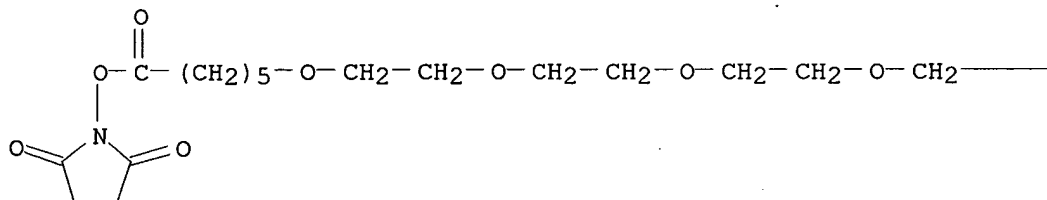
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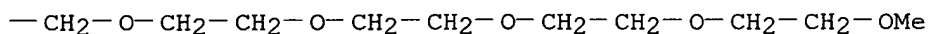
RN 477775-63-6 HCAPLUS

CN 2,5-Pyrrolidinedione, 1-[(1-oxo-7,10,13,16,19,22,25,28,31-nonaoxadotriacont-1-yl)oxy]- (9CI) (CA INDEX NAME)

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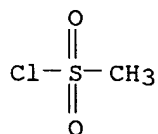
IT 124-63-0, Methanesulfonyl chloride

RL: RCT (Reactant); RACT (Reactant or reagent)

(methods of prep. monodispersed mixts. of polymers having polyethylene glycol moieties)

RN 124-63-0 HCAPLUS

CN Methanesulfonyl chloride (6CI, 8CI, 9CI) (CA INDEX NAME)



IT 7646-69-7, Sodium hydride

RL: RGT (Reagent); RACT (Reactant or reagent)
(methods of prep. monodispersed mixts. of polymers having polyethylene glycol moieties)

RN 7646-69-7 HCAPLUS

CN Sodium hydride (NaH) (8CI, 9CI) (CA INDEX NAME)

NaH

IT 100-44-7, Benzyl chloride, reactions 111-77-3,
Diethylene glycol monomethyl ether 112-35-6 112-60-7
2615-15-8 4792-15-8, 3,6,9,12-Tetraoxatetradecane-1,14-
diol 5299-60-5 6066-82-6, N-Hydroxysuccinimide

RL: RCT (Reactant); RACT (Reactant or reagent)
(starting materials; methods of prep. monodispersed mixts. of polymers
having polyethylene glycol moieties)

RN 100-44-7 HCAPLUS

CN Benzene, (chloromethyl)- (9CI) (CA INDEX NAME)

Ph-CH₂-Cl

RN 111-77-3 HCAPLUS

CN Ethanol, 2-(2-methoxyethoxy)- (6CI, 8CI, 9CI) (CA INDEX NAME)

MeO-CH₂-CH₂-O-CH₂-CH₂-OH

RN 112-35-6 HCAPLUS

CN Ethanol, 2-[2-(2-methoxyethoxy)ethoxy]- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

HO-CH₂-CH₂-O-CH₂-CH₂-O-CH₂-CH₂-OMe

RN 112-60-7 HCAPLUS

CN Ethanol, 2,2'-[oxybis(2,1-ethanediylloxy)]bis- (9CI) (CA INDEX NAME)

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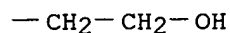
RN 2615-15-8 HCAPLUS

CN 3,6,9,12,15-Pentaoxaheptadecane-1,17-diol (9CI) (CA INDEX NAME)

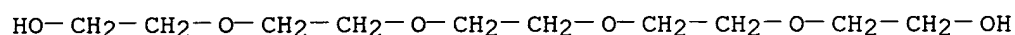
PAGE 1-A

HO-CH₂-CH₂-O-CH₂-CH₂-O-CH₂-CH₂-O-CH₂-CH₂-O-CH₂-CH₂-O-

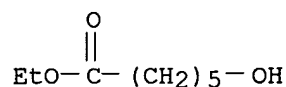
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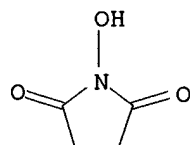
RN 4792-15-8 HCAPLUS
CN 3,6,9,12-Tetraoxatetradecane-1,14-diol (9CI) (CA INDEX NAME)



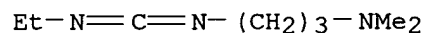
RN 5299-60-5 HCAPLUS
CN Hexanoic acid, 6-hydroxy-, ethyl ester (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



RN 6066-82-6 HCAPLUS
CN 2,5-Pyrrolidinedione, 1-hydroxy- (9CI) (CA INDEX NAME)



IT 25952-53-8, 1-(3-Dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride
RL: RGT (Reagent); RACT (Reactant or reagent)
(starting materials; methods of prep. monodispersed mixts. of polymers having polyethylene glycol moieties)
RN 25952-53-8 HCAPLUS
CN 1,3-Propanediamine, N'-(ethylcarbonimidoyl)-N,N-dimethyl-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:946135 HCAPLUS
DOCUMENT NUMBER: 138:16637
TITLE: Preparation of growth hormone drug-polyalkylene glycol

oligomer conjugates
 INVENTOR(S): Ekwuribe, Nnochiri N.; Price, Christopher H.; Ansari, Aslam M.; Odenbaugh, Amy L.
 PATENT ASSIGNEE(S): Nobex Corporation, USA
 SOURCE: PCT Int. Appl., 145 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002098452	A1	20021212	WO 2002-US17504	20020604
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003027995	A1	20030206	US 2001-873757	20010604

PRIORITY APPLN. INFO.:

US 2001-873757 A 20010604

OTHER SOURCE(S): MARPAT 138:16637

AB A mixt. of conjugates in which each conjugate in the mixt. comprises a growth hormone drug coupled to an oligomer that includes a polyalkylene glycol moiety is disclosed. Thus, non-polydispersed hexaethylene glycol was treated with phosgene soln., followed by treatment with N-hydroxysuccinimide (NHS) to give the NHS ester. Human growth hormone (Saizen) was dissolved in DMSO and allowed to react with the NHS ester to give the conjugate.

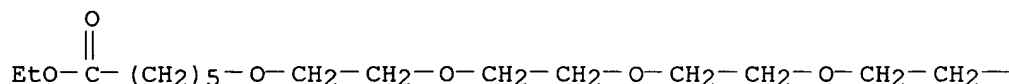
IT 477775-58-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (hydrogenolysis of; prepn. of growth hormone drug-polyalkylene glycol oligomer conjugates)

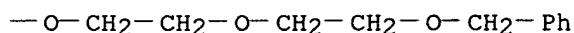
RN 477775-58-9 HCAPLUS

CN 2,5,8,11,14,17,20-Heptaohexacosan-26-oic acid, 1-phenyl-, ethyl ester (9CI) (CA INDEX NAME)

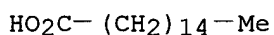
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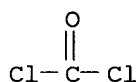
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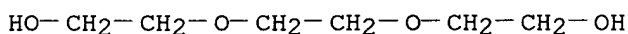
IT 57-10-3, Hexadecanoic acid, reactions 75-44-5, Phosgene
 112-27-6 112-35-6 112-60-7, Tetraethylene
 glycol 112-76-5, Octadecanoyl chloride 1679-53-4,
 10-Hydroxydecanoic acid 2615-15-8 3639-35-8
 5299-60-5, Ethyl 6-hydroxyhexanoate 6066-82-6,
 N-Hydroxysuccinimide 17696-11-6 25322-68-3,
 Polyethylene glycol 74124-79-1 86259-87-2
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (in alkylene glycol derivs. prepn.; prepn. of growth hormone
 drug-polyalkylene glycol oligomer conjugates)
 RN 57-10-3 HCAPLUS
 CN Hexadecanoic acid (9CI) (CA INDEX NAME)



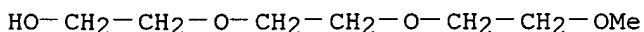
RN 75-44-5 HCAPLUS
 CN Carbonic dichloride (9CI) (CA INDEX NAME)



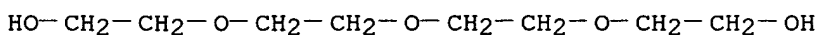
RN 112-27-6 HCAPLUS
 CN Ethanol, 2,2'-[1,2-ethanediylbis(oxy)]bis- (9CI) (CA INDEX NAME)



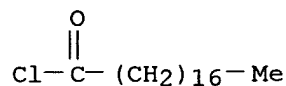
RN 112-35-6 HCAPLUS
 CN Ethanol, 2-[2-(2-methoxyethoxy)ethoxy]- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



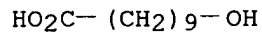
RN 112-60-7 HCAPLUS
 CN Ethanol, 2,2'-[oxybis(2,1-ethanediylloxy)]bis- (9CI) (CA INDEX NAME)



RN 112-76-5 HCAPLUS
 CN Octadecanoyl chloride (9CI) (CA INDEX NAME)

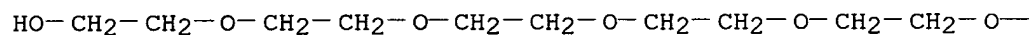


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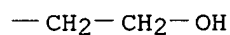


RN 2615-15-8 HCAPLUS
CN 3,6,9,12,15-Pentaoxaheptadecane-1,17-diol (9CI) (CA INDEX NAME)

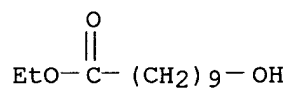
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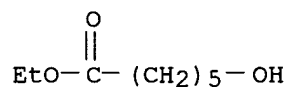
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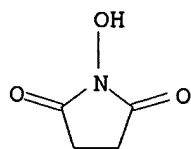
RN 3639-35-8 HCAPLUS
CN Decanoic acid, 10-hydroxy-, ethyl ester (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



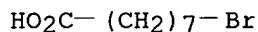
RN 5299-60-5 HCAPLUS
CN Hexanoic acid, 6-hydroxy-, ethyl ester (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



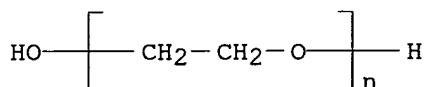
RN 6066-82-6 HCAPLUS
CN 2,5-Pyrrolidinedione, 1-hydroxy- (9CI) (CA INDEX NAME)



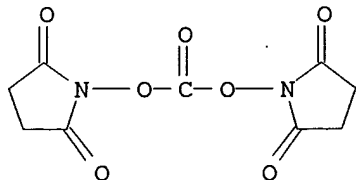
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CN Octanoic acid, 8-bromo- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



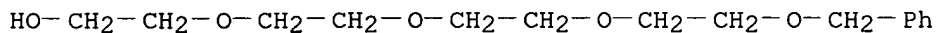
RN 25322-68-3 HCAPLUS
CN Poly(oxy-1,2-ethanediyl), .alpha.-hydro-.omega.-hydroxy- (9CI) (CA INDEX NAME)



RN 74124-79-1 HCAPLUS
CN 2,5-Pyrrolidinedione, 1,1'-[carbonylbis(oxy)]bis- (9CI) (CA INDEX NAME)



RN 86259-87-2 HCAPLUS
CN 2,5,8,11-Tetraoxatridecan-13-ol, 1-phenyl- (9CI) (CA INDEX NAME)

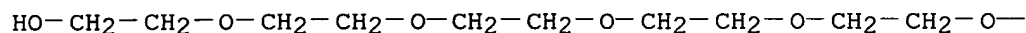


IT 4437-01-8P, 2,5,8,11,14,17,20-Heptaoadocosan-22-ol
9004-99-3P 29823-21-0P 51023-28-0P
62304-85-2P 70802-40-3P 74654-05-0P
87117-61-1P 105292-71-5P 124668-93-5P
477775-57-8P 477775-59-0P 477775-60-3P
477775-61-4P 477775-62-5P 477775-64-7P
477775-65-8P 477775-67-0P 477775-68-1P
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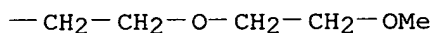
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(in alkylene glycol derivs. prepn.; prepn. of growth hormone drug-polyalkylene glycol oligomer conjugates)

RN 4437-01-8 HCAPLUS
CN 2,5,8,11,14,17,20-Heptaoadocosan-22-ol (6CI, 8CI, 9CI) (CA INDEX NAME)

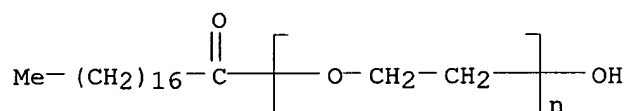
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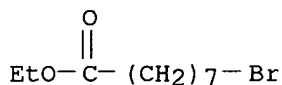
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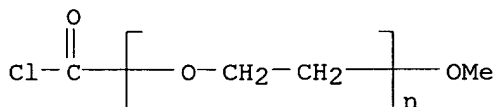
RN 9004-99-3 HCAPLUS
CN Poly(oxy-1,2-ethanediyl), .alpha.-(1-oxooctadecyl)-.omega.-hydroxy- (9CI)
(CA INDEX NAME)



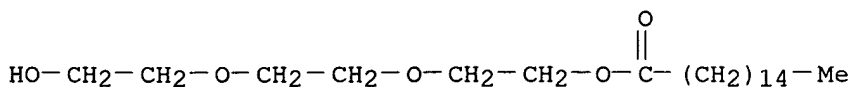
RN 29823-21-0 HCAPLUS
CN Octanoic acid, 8-bromo-, ethyl ester (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



RN 51023-28-0 HCAPLUS
CN Poly(oxy-1,2-ethanediyl), .alpha.-(chlorocarbonyl)-.omega.-methoxy- (9CI)
(CA INDEX NAME)



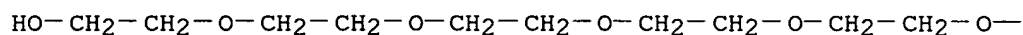
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CN Hexadecanoic acid, 2-[2-(2-hydroxyethoxy)ethoxy]ethyl ester (9CI) (CA INDEX NAME)



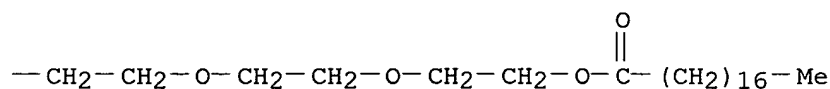
RN 70802-40-3 HCAPLUS
CN Octadecanoic acid, 23-hydroxy-3,6,9,12,15,18,21-heptaotricos-1-yl ester

(9CI) (CA INDEX NAME)

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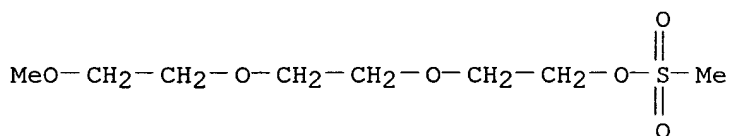


PAGE 1-B



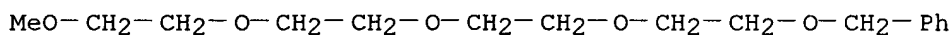
RN 74654-05-0 HCAPLUS

CN Ethanol, 2-[2-(2-methoxyethoxy)ethoxy]-, methanesulfonate (9CI) (CA INDEX NAME)



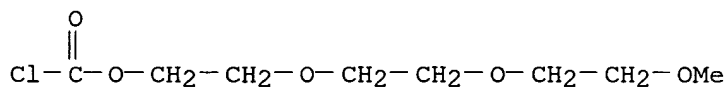
RN 87117-61-1 HCAPLUS

CN 2,5,8,11,14-Pentaoxapentadecane, 1-phenyl- (9CI) (CA INDEX NAME)



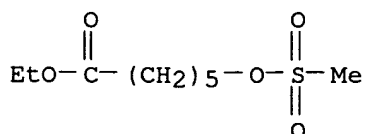
RN 105292-71-5 HCAPLUS

CN Carbonochloridic acid, 2-[2-(2-methoxyethoxy)ethoxy]ethyl ester (9CI) (CA INDEX NAME)



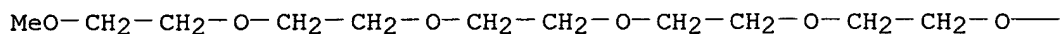
RN 124668-93-5 HCAPLUS

CN Hexanoic acid, 6-[(methylsulfonyl)oxy]-, ethyl ester (9CI) (CA INDEX NAME)

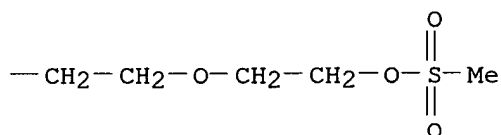


RN 477775-57-8 HCAPLUS
CN 2,5,8,11,14,17,20-Heptaoxidocosan-22-ol, methanesulfonate (9CI) (CA INDEX NAME)

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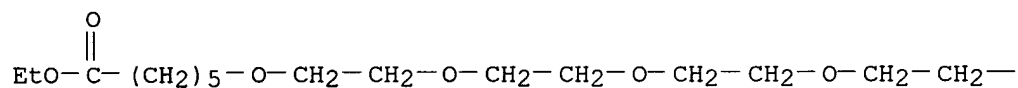


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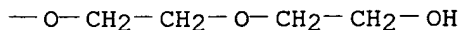


RN 477775-59-0 HCAPLUS
CN 3,6,9,12,15,18-Hexaoxatetracosan-24-oic acid, 1-hydroxy-, ethyl ester (9CI) (CA INDEX NAME)

PAGE 1-A

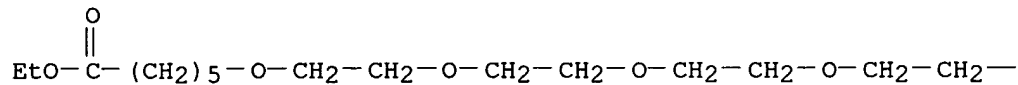


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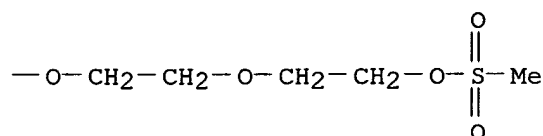


RN 477775-60-3 HCAPLUS
CN 3,6,9,12,15,18-Hexaoxatetracosan-24-oic acid, 1-[(methylsulfonyl)oxy]-, ethyl ester (9CI) (CA INDEX NAME)

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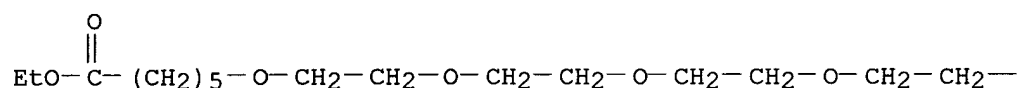


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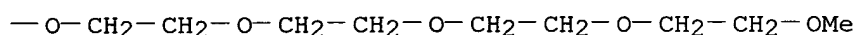


RN 477775-61-4 HCAPLUS
CN 2,5,8,11,14,17,20,23,26-Nonaoxadotriacontan-32-oic acid, ethyl ester (9CI)
(CA INDEX NAME)

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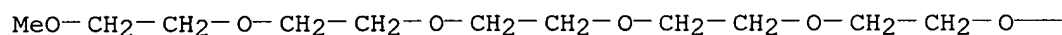


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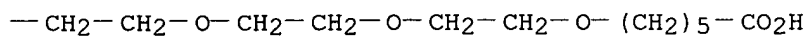


RN 477775-62-5 HCAPLUS
CN 2,5,8,11,14,17,20,23,26-Nonaoxadotriacontan-32-oic acid (9CI) (CA INDEX NAME)

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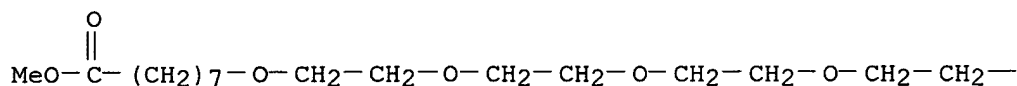


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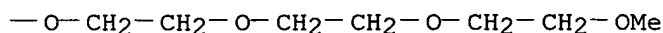


RN 477775-64-7 HCAPLUS
CN 2,5,8,11,14,17,20,23-Octaoxahentriacontan-31-oic acid, methyl ester (9CI)
(CA INDEX NAME)

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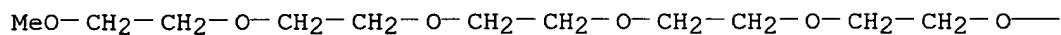


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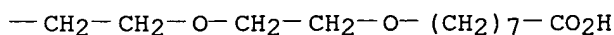


RN 477775-65-8 HCAPLUS
CN 2,5,8,11,14,17,20,23-Octaoxahentriacontan-31-oic acid (9CI) (CA INDEX NAME)

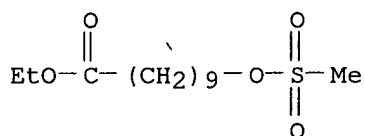
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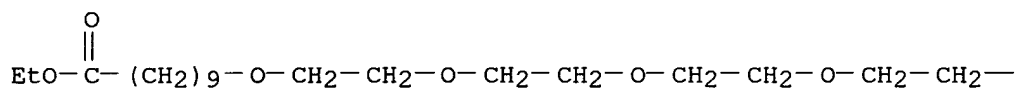


RN 477775-67-0 HCAPLUS
CN Decanoic acid, 10-[(methylsulfonyl)oxy]-, ethyl ester (9CI) (CA INDEX NAME)

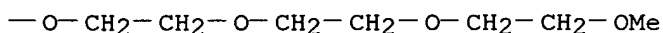


RN 477775-68-1 HCAPLUS
CN 2,5,8,11,14,17,20,23-Octaoxatritriacontan-33-oic acid, ethyl ester (9CI) (CA INDEX NAME)

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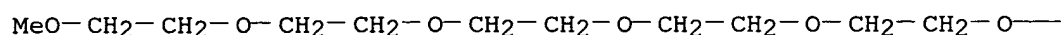


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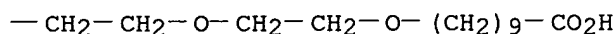


RN 477775-69-2 HCAPLUS
CN 2,5,8,11,14,17,20,23-Octaoxatritriacontan-33-oic acid (9CI) (CA INDEX NAME)

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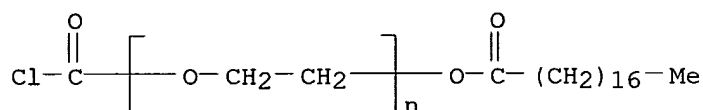


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RN 477775-71-6 HCAPLUS

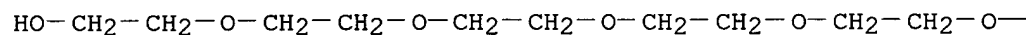
CN Poly(oxy-1,2-ethanediyl), .alpha.-(chlorocarbonyl)-.omega.-[(1-oxooctadecyl)oxy]- (9CI) (CA INDEX NAME)



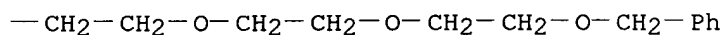
RN 477775-73-8 HCAPLUS

CN 2,5,8,11,14,17,20,23-Octaoxapentacosan-25-ol, 1-phenyl- (9CI) (CA INDEX NAME)

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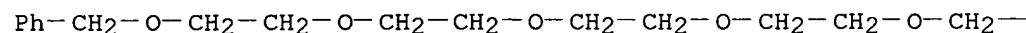
PAGE 1-B



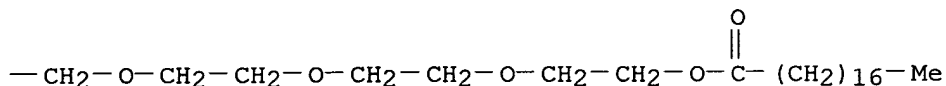
RN 477775-74-9 HCAPLUS

CN Octadecanoic acid, 25-phenyl-3,6,9,12,15,18,21,24-octaoxapentacos-1-yl ester (9CI) (CA INDEX NAME)

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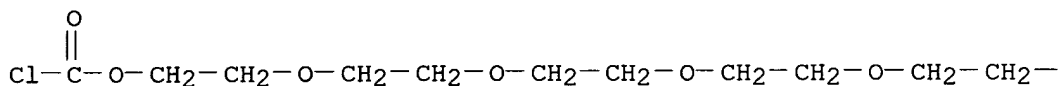
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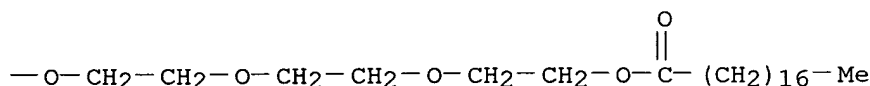
RN 477775-75-0 HCAPLUS

CN Octadecanoic acid, 25-chloro-25-oxo-3,6,9,12,15,18,21,24-octaoxapentacos-1-yl ester (9CI) (CA INDEX NAME)

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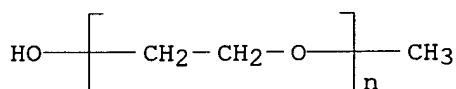
IT 9004-74-4P, Monomethoxy polyethylene glycol

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(mesylation as esterification reactions of; prepn. of growth hormone drug-polyalkylene glycol oligomer conjugates)

RN 9004-74-4 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), .alpha.-methyl-.omega.-hydroxy- (9CI) (CA INDEX NAME)



IT 24342-68-5P 135649-01-3P 259228-98-3P

477775-63-6P 477775-66-9P 477775-70-5P

477775-72-7P 477775-76-1P 477775-77-2P

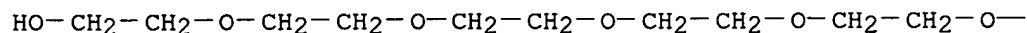
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of growth hormone drug-polyalkylene glycol oligomer conjugates)

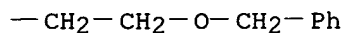
RN 24342-68-5 HCAPLUS

CN 2,5,8,11,14,17-Hexaoxanonadecan-19-ol, 1-phenyl- (9CI) (CA INDEX NAME)

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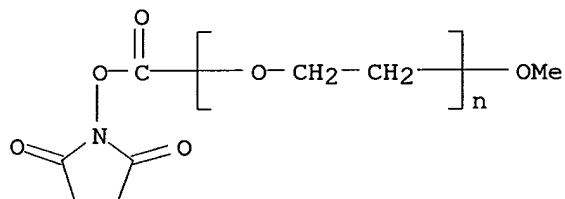


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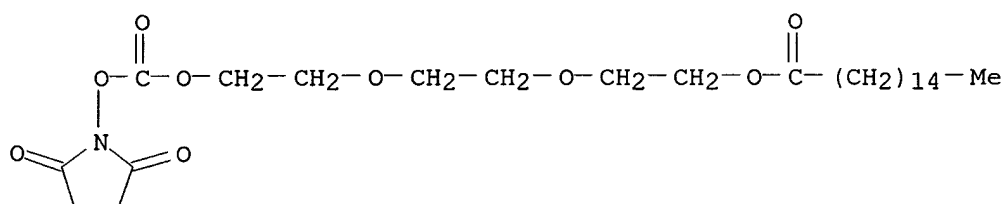
RN 135649-01-3 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), .alpha.-[[(2,5-dioxo-1-pyrrolidinyl)oxy]carbonyl]-.omega.-methoxy- (9CI) (CA INDEX NAME)



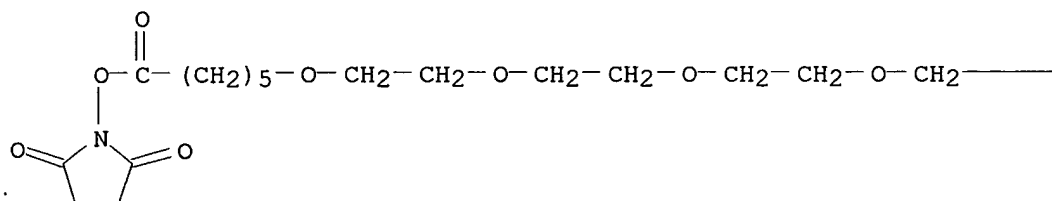
RN 259228-98-3 HCAPLUS

CN Hexadecanoic acid, 2-[2-[2-[[(2,5-dioxo-1-pyrrolidinyl)oxy]carbonyl]oxy]ethoxy]ethoxy]ethyl ester (9CI) (CA INDEX NAME)



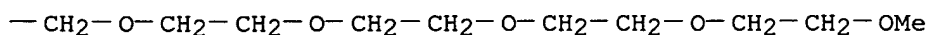
RN 477775-63-6 HCAPLUS

CN 2,5-Pyrrolidinedione, 1-[(1-oxo-7,10,13,16,19,22,25,28,31-nonaaxadotriacont-1-yl)oxy]- (9CI) (CA INDEX NAME)



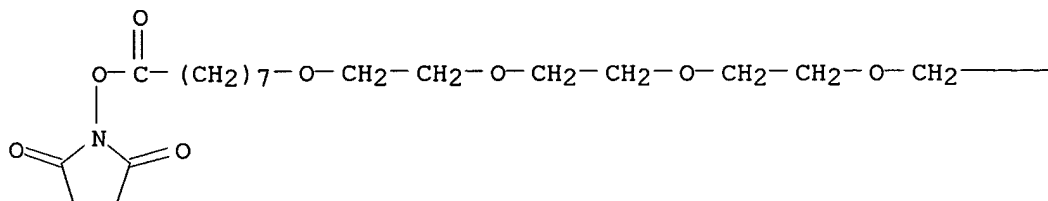
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RN 477775-66-9 HCAPLUS
 CN 2,5-Pyrrolidinedione, 1-[(1-oxo-9,12,15,18,21,24,27,30-octaoxahentriacont-1-yl)oxy]- (9CI) (CA INDEX NAME)

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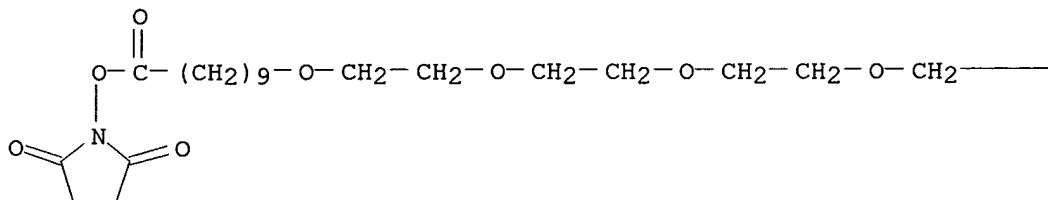


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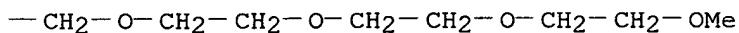


RN 477775-70-5 HCAPLUS
 CN 2,5-Pyrrolidinedione, 1-[(1-oxo-11,14,17,20,23,26,29,32-octaoxatritriacont-1-yl)oxy]- (9CI) (CA INDEX NAME)

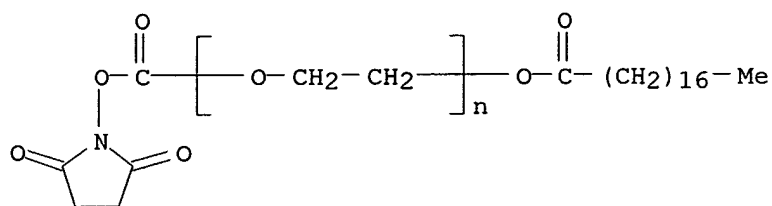
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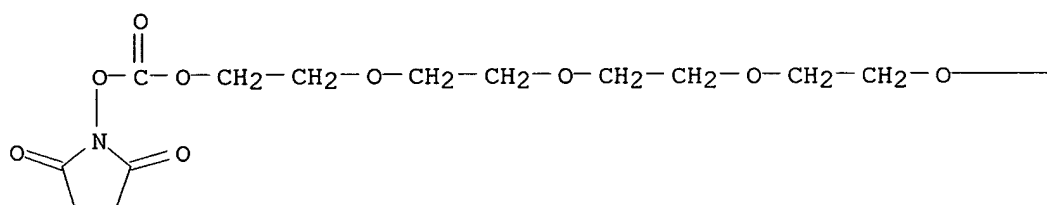


RN 477775-72-7 HCAPLUS
 CN Poly(oxy-1,2-ethanediyl), .alpha.-[[(2,5-dioxo-1-pyrrolidinyl)oxy]carbonyl]-.omega.-[(1-oxooctadecyl)oxy]- (9CI) (CA INDEX NAME)

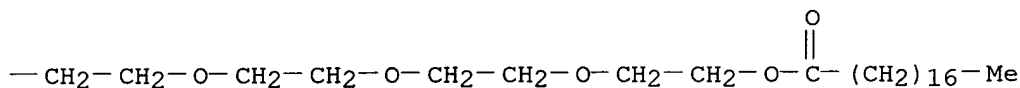


RN 477775-76-1 HCAPLUS
 CN Octadecanoic acid, 25-[(2,5-dioxo-1-pyrrolidinyloxy)-25-oxo-3,6,9,12,15,18,21,24-octaoxapentacos-1-yl ester (9CI) (CA INDEX NAME)

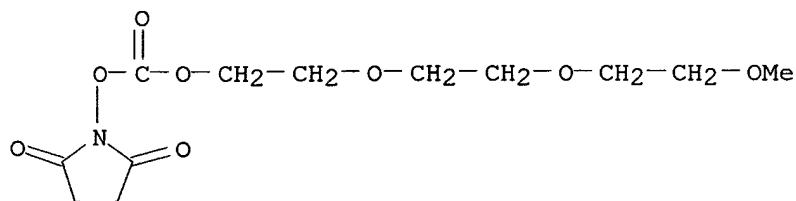
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RN 477775-77-2 HCAPLUS
 CN 2,5-Pyrrolidinedione, 1-[(1-oxo-2,5,8,11-tetraoxadodec-1-yl)oxy]- (9CI)
 (CA INDEX NAME)



IT 9002-72-6DP, Growth hormone, conjugates with polyalkylene glycols
 12629-01-5DP, Saizen, conjugates with polyalkylene glycols
 135649-01-3DP, conjugates with growth hormone
 259228-98-3DP, conjugates with growth hormone
 477775-63-6DP, conjugates with growth hormone
 477775-66-9DP, conjugates with growth hormone
 477775-70-5DP, conjugates with growth hormone
 477775-72-7DP, conjugates with growth hormone
 477775-76-1DP, conjugates with growth hormone
 477775-77-2DP, conjugates with growth hormone

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of growth hormone drug-polyalkylene glycol oligomer conjugates)

RN 9002-72-6 HCAPLUS

CN Somatotropin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

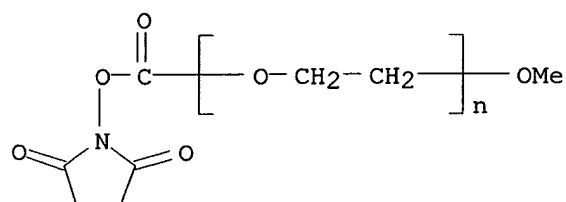
RN 12629-01-5 HCAPLUS

CN Somatotropin (human) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

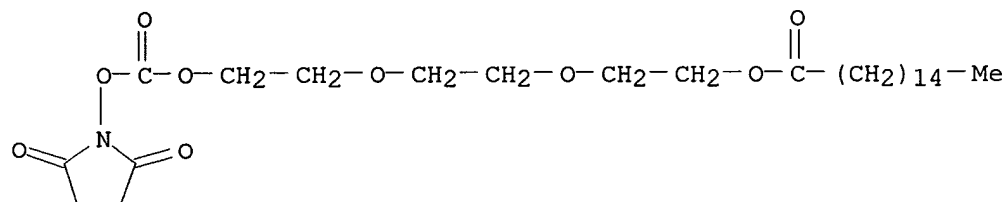
RN 135649-01-3 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), .alpha.-[[(2,5-dioxo-1-pyrrolidinyloxy)carbonyl]-.omega.-methoxy- (9CI) (CA INDEX NAME)



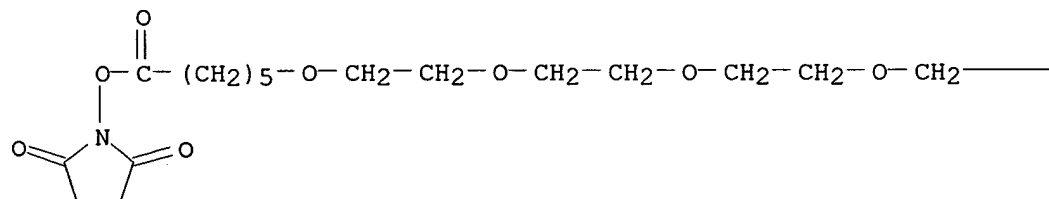
RN 259228-98-3 HCAPLUS

CN Hexadecanoic acid, 2-[2-[2-[[[(2,5-dioxo-1-pyrrolidinyloxy)carbonyl]oxy]ethoxy]ethoxy]ethyl ester (9CI) (CA INDEX NAME)



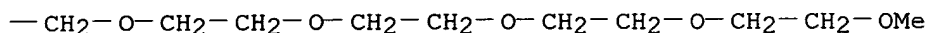
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CN 2,5-Pyrrolidinedione, 1-[(1-oxo-7,10,13,16,19,22,25,28,31-nonaoxadotriacont-1-yl)oxy]- (9CI) (CA INDEX NAME)



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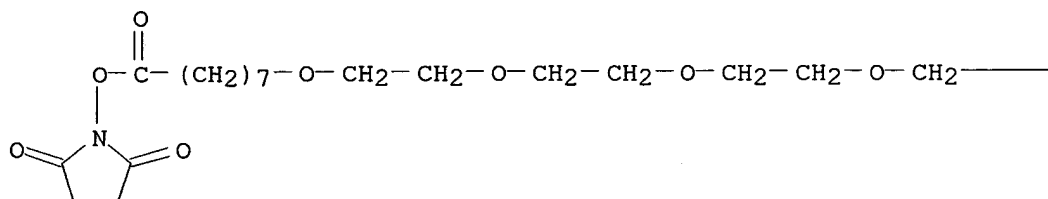
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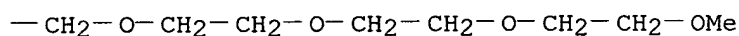
RN 477775-66-9 HCAPLUS

CN 2,5-Pyrrolidinedione, 1-[(1-oxo-9,12,15,18,21,24,27,30-octaoxahentriacont-1-yl)oxy]- (9CI) (CA INDEX NAME)

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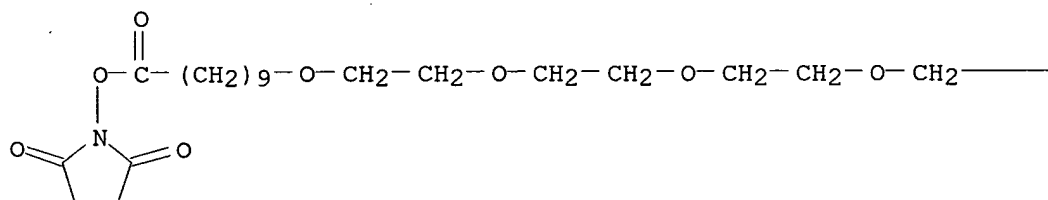
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RN 477775-70-5 HCAPLUS

CN 2,5-Pyrrolidinedione, 1-[(1-oxo-11,14,17,20,23,26,29,32-octaoxatritriacont-1-yl)oxy]- (9CI) (CA INDEX NAME)

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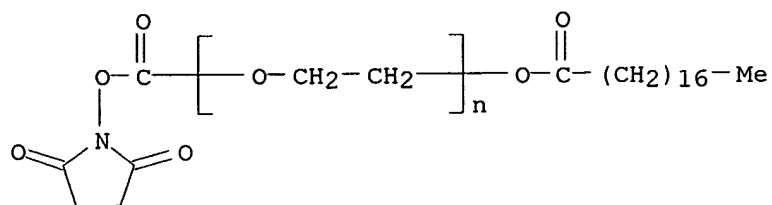
PAGE 1-B



RN 477775-72-7 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), .alpha.-[[(2,5-dioxo-1-

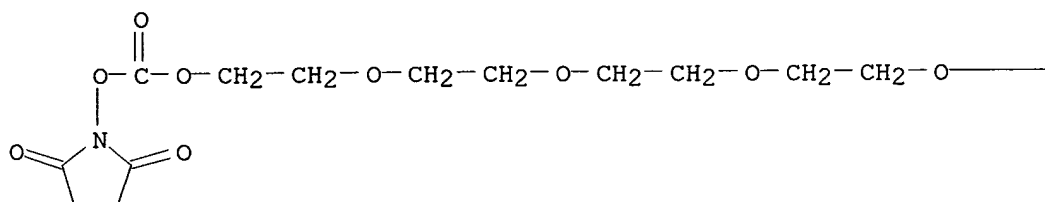
pyrrolidinyl)oxy]carbonyl]-.omega.-[(1-oxooctadecyl)oxy]- (9CI) (CA INDEX NAME)



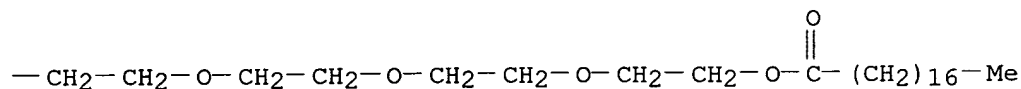
RN 477775-76-1 HCAPLUS

CN Octadecanoic acid, 25-[(2,5-dioxo-1-pyrrolidinyl)oxy]-25-oxo-3,6,9,12,15,18,21,24-octa-oxapentacos-1-yl ester (9CI) (CA INDEX NAME)

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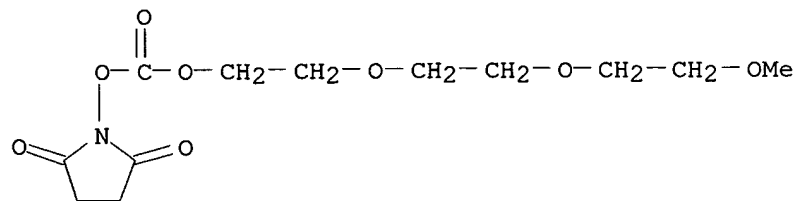


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RN 477775-77-2 HCAPLUS

CN 2,5-Pyrrolidinedione, 1-[(1-oxo-2,5,8,11-tetraoxadodec-1-yl)oxy]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:946134 HCAPLUS

DOCUMENT NUMBER: 138:16636

TITLE: Preparation of calcitonin drug-alkylene glycol

INVENTOR(S): oligomer conjugates
Ekwuribe, Nnochiri N.; Price, Christopher H.; Ansari, Aslam M.; Odenbaugh, Amy L.
 PATENT ASSIGNEE(S): Nobex Corporation, USA
 SOURCE: PCT Int. Appl., 126 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002098451	A1	20021212	WO 2002-US17575	20020604
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: US 2001-873777 A 20010604

OTHER SOURCE(S): MARPAT 138:16636

AB A mixt. of conjugates in which each conjugate in the mixt. comprises a calcitonin drug coupled to an oligomer that includes a polyalkylene glycol moiety is disclosed. The mixt. may lower serum calcium levels in a subject by 10, 15 or .gtoreq.20%. Moreover, the mixt. may be more effective at surviving an in vitro model of intestinal digestion than non-conjugated calcitonin. Furthermore, the mixt. may exhibit a higher bioavailability than the non-conjugated calcitonin. Thus, non-polydispersed hexaethylene glycol was treated with phosgene soln., followed by treatment with N-hydroxysuccinimide (NHS) to give the NHS ester. Salmon calcitonin was allowed to react with the NHS ester to give the conjugate.

IT 7440-70-2, Calcium, biological studies
 RL: ADV (Adverse effect, including toxicity); BIOL (Biological study) (hypercalcemia; prepn. of calcitonin drug-alkylene glycol oligomer conjugates)

RN 7440-70-2 HCAPLUS

CN Calcium (8CI, 9CI) (CA INDEX NAME)

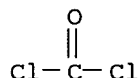
Ca

IT 57-10-3, Palmitic acid, reactions 75-44-5, Phosgene
 111-77-3 112-27-6, Triethylene glycol 112-35-6
 112-60-7, Tetraethylene glycol 112-76-5, Octadecanoyl chloride 2615-15-8 5299-60-5, Ethyl 6-hydroxyhexanoate 6066-82-6, N-Hydroxysuccinimide 17696-11-6
 25322-68-3, Polyethylene glycol 74124-79-1
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (in alkylene glycol oligomers prepn.; prepn. of calcitonin drug-alkylene glycol oligomer conjugates)

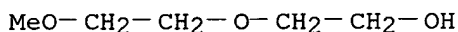
RN 57-10-3 HCAPLUS
CN Hexadecanoic acid (9CI) (CA INDEX NAME)



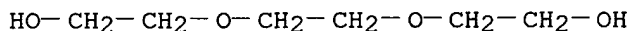
RN 75-44-5 HCAPLUS
CN Carbonic dichloride (9CI) (CA INDEX NAME)



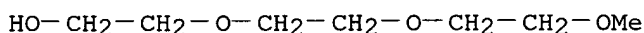
RN 111-77-3 HCAPLUS
CN Ethanol, 2-(2-methoxyethoxy)- (6CI, 8CI, 9CI) (CA INDEX NAME)



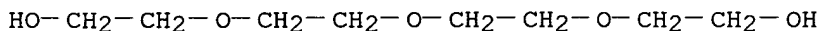
RN 112-27-6 HCAPLUS
CN Ethanol, 2,2'-[1,2-ethanediylbis(oxy)]bis- (9CI) (CA INDEX NAME)



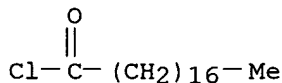
RN 112-35-6 HCAPLUS
CN Ethanol, 2-[2-(2-methoxyethoxy)ethoxy]- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



RN 112-60-7 HCAPLUS
CN Ethanol, 2,2'-[oxybis(2,1-ethanediylxy)]bis- (9CI) (CA INDEX NAME)

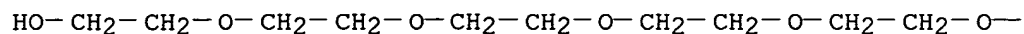


RN 112-76-5 HCAPLUS
CN Octadecanoyl chloride (9CI) (CA INDEX NAME)

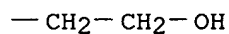


RN 2615-15-8 HCAPLUS
CN 3,6,9,12,15-Pentaoxaheptadecane-1,17-diol (9CI) (CA INDEX NAME)

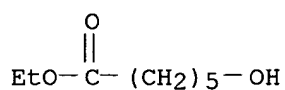
PAGE 1-A



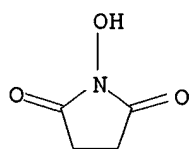
PAGE 1-B



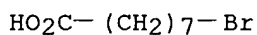
RN 5299-60-5 HCAPLUS
CN Hexanoic acid, 6-hydroxy-, ethyl ester (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



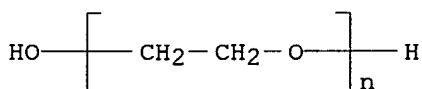
RN 6066-82-6 HCAPLUS
CN 2,5-Pyrrolidinedione, 1-hydroxy- (9CI) (CA INDEX NAME)



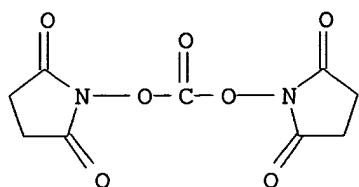
RN 17696-11-6 HCAPLUS
CN Octanoic acid, 8-bromo- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



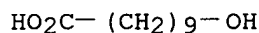
RN 25322-68-3 HCAPLUS
CN Poly(oxy-1,2-ethanediyl), .alpha.-hydro-.omega.-hydroxy- (9CI) (CA INDEX NAME)



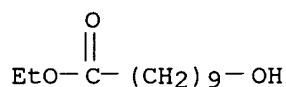
RN 74124-79-1 HCAPLUS
CN 2,5-Pyrrolidinedione, 1,1'-[carbonylbis(oxy)]bis- (9CI) (CA INDEX NAME)



IT 1679-53-4P, 10-Hydroxydecanoic acid 3639-35-8P
 4437-01-8P, 2,5,8,11,14,17,20-Heptaadecan-22-ol
 9004-74-4P, Monomethoxy polyethylene glycol 9004-99-3P
 24342-68-5P 29823-21-0P 51023-28-0P
 62304-85-2P 70802-40-3P 74654-05-0P
 86259-87-2P 105292-71-5P 124668-93-5P
 175172-61-9P 477775-58-9P 477775-59-0P
 477775-60-3P 477775-61-4P 477775-62-5P
 477775-65-8P 477775-67-0P 477775-68-1P
 477775-69-2P 477775-71-6P 477775-73-8P
 477775-74-9P 477775-75-0P 477775-77-2P
 477781-68-3P 477781-69-4P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)
 (in alkylene glycol oligomers prepn.; prepn. of calcitonin
 drug-alkylene glycol oligomer conjugates)
 RN 1679-53-4 HCAPLUS
 CN Decanoic acid, 10-hydroxy- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

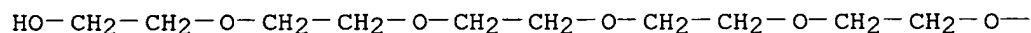


RN 3639-35-8 HCAPLUS
 CN Decanoic acid, 10-hydroxy-, ethyl ester (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

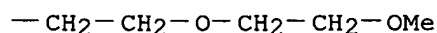


RN 4437-01-8 HCAPLUS
 CN 2,5,8,11,14,17,20-Heptaadecan-22-ol (6CI, 8CI, 9CI) (CA INDEX NAME)

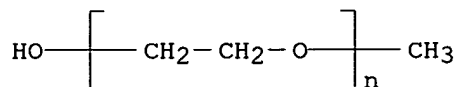
PAGE 1-A



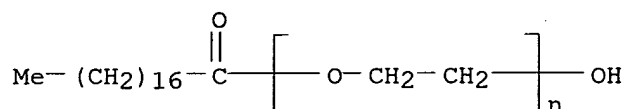
PAGE 1-B



RN 9004-74-4 HCAPLUS
CN Poly(oxy-1,2-ethanediyl), .alpha.-methyl-.omega.-hydroxy- (9CI) (CA INDEX NAME)

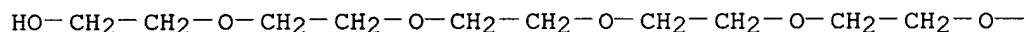


RN 9004-99-3 HCAPLUS
CN Poly(oxy-1,2-ethanediyl), .alpha.-(1-oxooctadecyl)-.omega.-hydroxy- (9CI) (CA INDEX NAME)

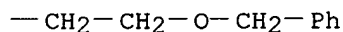


RN 24342-68-5 HCAPLUS
CN 2,5,8,11,14,17-Hexaoxonadecan-19-ol, 1-phenyl- (9CI) (CA INDEX NAME)

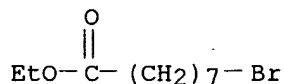
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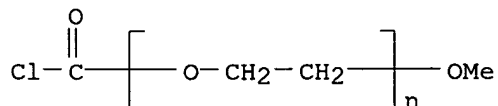
PAGE 1-B



RN 29823-21-0 HCAPLUS
CN Octanoic acid, 8-bromo-, ethyl ester (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

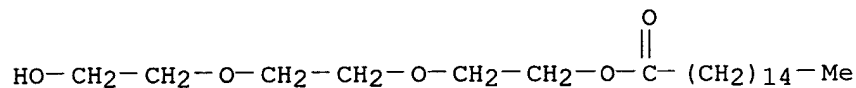


RN 51023-28-0 HCAPLUS
CN Poly(oxy-1,2-ethanediyl), .alpha.-(chlorocarbonyl)-.omega.-methoxy- (9CI) (CA INDEX NAME)



RN 62304-85-2 HCAPLUS
CN Hexadecanoic acid, 2-[2-(2-hydroxyethoxy)ethoxy]ethyl ester (9CI) (CA

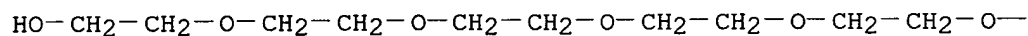
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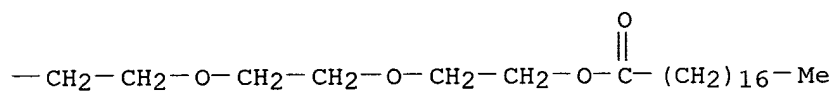
RN 70802-40-3 HCAPLUS

CN Octadecanoic acid, 23-hydroxy-3,6,9,12,15,18,21-heptaoxatricos-1-yl ester
(9CI) (CA INDEX NAME)

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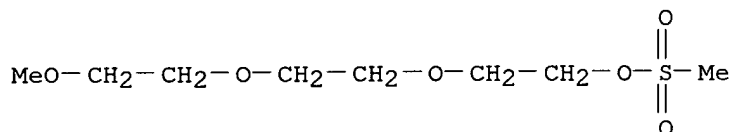


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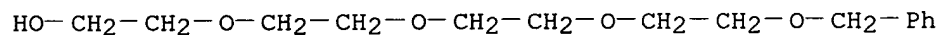
RN 74654-05-0 HCAPLUS

CN Ethanol, 2-[2-(2-methoxyethoxy)ethoxy]-, methanesulfonate (9CI) (CA INDEX NAME)



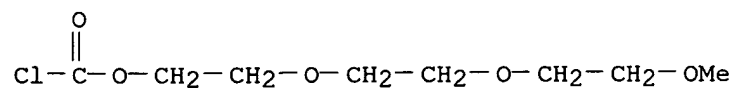
RN 86259-87-2 HCAPLUS

CN 2,5,8,11-Tetraoxatridecan-13-ol, 1-phenyl- (9CI) (CA INDEX NAME)



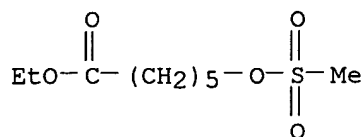
RN 105292-71-5 HCAPLUS

CN Carbonochloridic acid, 2-[2-(2-methoxyethoxy)ethoxy]ethyl ester (9CI) (CA INDEX NAME)



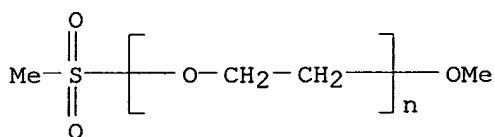
RN 124668-93-5 HCAPLUS

CN Hexanoic acid, 6-[(methylsulfonyl)oxy]-, ethyl ester (9CI) (CA INDEX NAME)



RN 175172-61-9 HCAPLUS

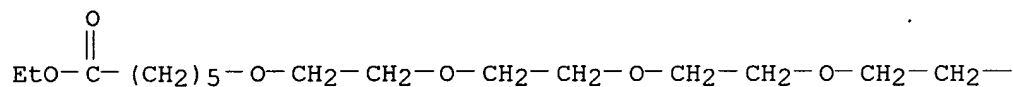
CN Poly(oxy-1,2-ethanediyl), .alpha.-(methylsulfonyl)-.omega.-methoxy- (9CI)
(CA INDEX NAME)



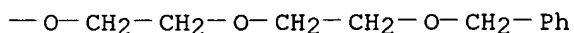
RN 477775-58-9 HCAPLUS

CN 2,5,8,11,14,17,20-Heptaohexacosan-26-oic acid, 1-phenyl-, ethyl ester
(9CI) (CA INDEX NAME)

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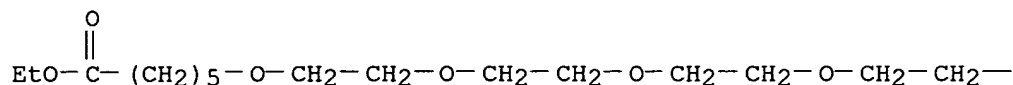
PAGE 1-B



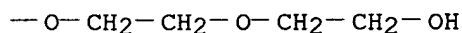
RN 477775-59-0 HCAPLUS

CN 3,6,9,12,15,18-Hexaoxatetracosan-24-oic acid, 1-hydroxy-, ethyl ester
(9CI) (CA INDEX NAME)

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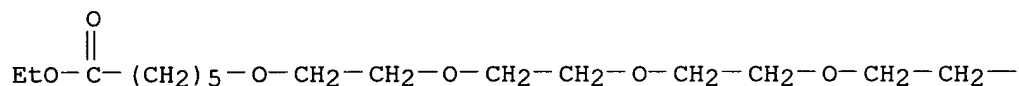


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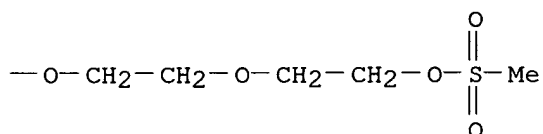


RN 477775-60-3 HCAPLUS
CN 3,6,9,12,15,18-Hexaoxatetracosan-24-oic acid, 1-[(methylsulfonyl)oxy]-, ethyl ester (9CI) (CA INDEX NAME)

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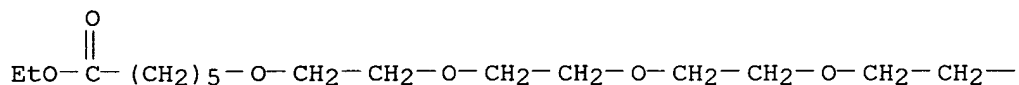


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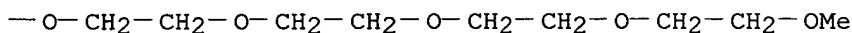


RN 477775-61-4 HCAPLUS
CN 2,5,8,11,14,17,20,23,26-Nonaoxadotriacontan-32-oic acid, ethyl ester (9CI) (CA INDEX NAME)

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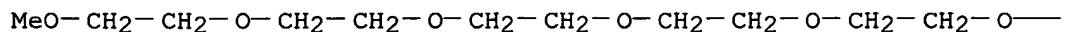


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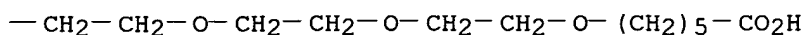


RN 477775-62-5 HCAPLUS
CN 2,5,8,11,14,17,20,23,26-Nonaoxadotriacontan-32-oic acid (9CI) (CA INDEX NAME)

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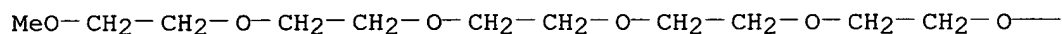
PAGE 1-B



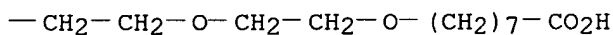
RN 477775-65-8 HCAPLUS

CN 2,5,8,11,14,17,20,23-Octaoxahentriacontan-31-oic acid (9CI) (CA INDEX NAME)

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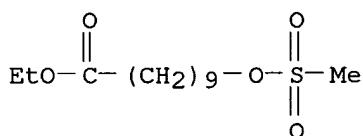


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RN 477775-67-0 HCAPLUS

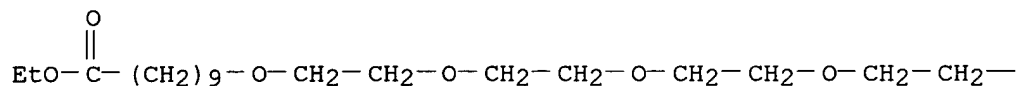
CN Decanoic acid, 10-[(methylsulfonyl)oxy]-, ethyl ester (9CI) (CA INDEX NAME)



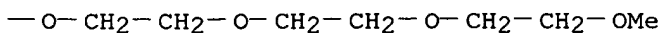
RN 477775-68-1 HCAPLUS

CN 2,5,8,11,14,17,20,23-Octaoxatritriacontan-33-oic acid, ethyl ester (9CI) (CA INDEX NAME)

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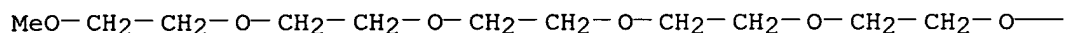
PAGE 1-B



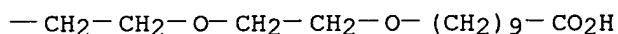
RN 477775-69-2 HCAPLUS

CN 2,5,8,11,14,17,20,23-Octaoxatritriacontan-33-oic acid (9CI) (CA INDEX NAME)

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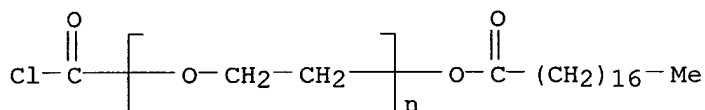


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RN 477775-71-6 HCAPLUS

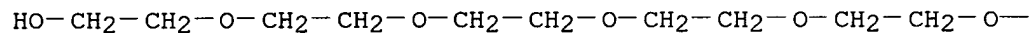
CN Poly(oxy-1,2-ethanediyl), .alpha.-(chlorocarbonyl)-.omega.-[(1-oxooctadecyl)oxy]- (9CI) (CA INDEX NAME)



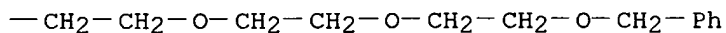
RN 477775-73-8 HCAPLUS

CN 2,5,8,11,14,17,20,23-Octaoxapentacosan-25-ol, 1-phenyl- (9CI) (CA INDEX NAME)

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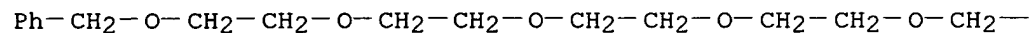
PAGE 1-B



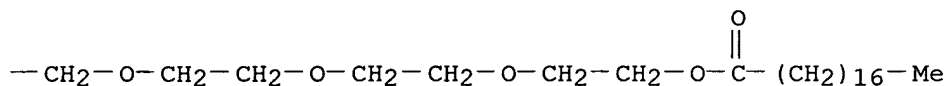
RN 477775-74-9 HCAPLUS

CN Octadecanoic acid, 25-phenyl-3,6,9,12,15,18,21,24-octaoxapentacos-1-yl ester (9CI) (CA INDEX NAME)

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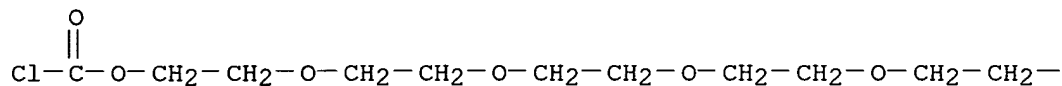
PAGE 1-B



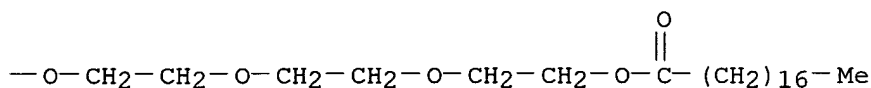
RN 477775-75-0 HCAPLUS

CN Octadecanoic acid, 25-chloro-25-oxo-3,6,9,12,15,18,21,24-octaoxapentacos-1-yl ester (9CI) (CA INDEX NAME)

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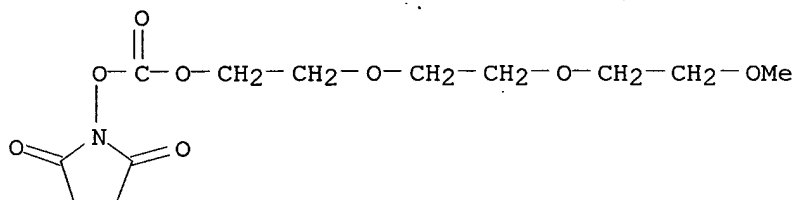


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RN 477775-77-2 HCAPLUS

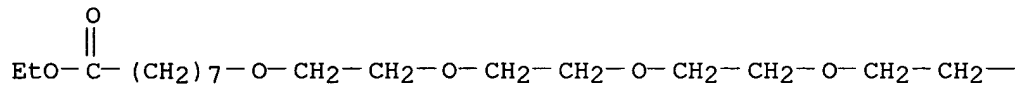
CN 2,5-Pyrrolidinedione, 1-[(1-oxo-2,5,8,11-tetraoxadodec-1-yl)oxy]- (9CI) (CA INDEX NAME)



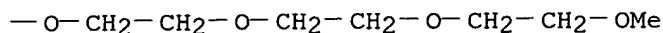
RN 477781-68-3 HCAPLUS

CN 2,5,8,11,14,17,20,23-Octaoxahentriacontan-31-oic acid, ethyl ester (9CI) (CA INDEX NAME)

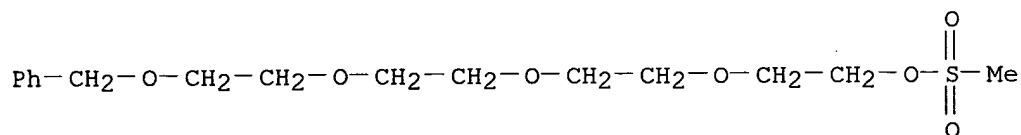
PAGE 1-A



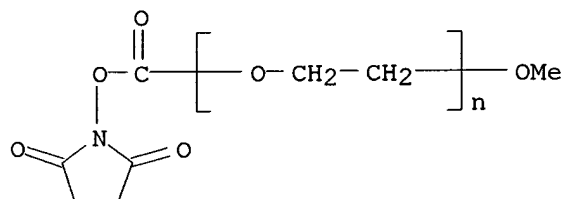
PAGE 1-B



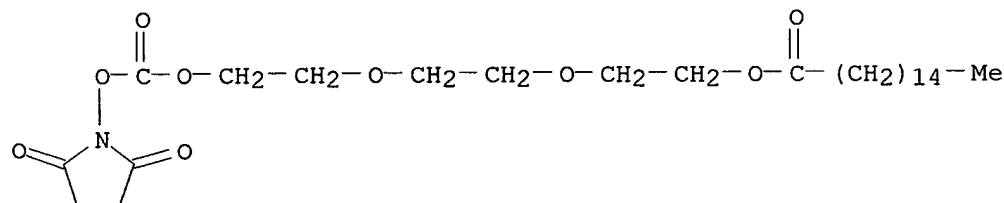
RN 477781-69-4 HCAPLUS
 CN 2,5,8,11-Tetraoxatridecan-13-ol, 1-phenyl-, methanesulfonate (9CI) (CA INDEX NAME)



IT 135649-01-3P 259228-98-3P 477775-63-6P
 477775-66-9P 477775-70-5P 477775-72-7P
 477775-76-1P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (prepn. of calcitonin drug-alkylene glycol oligomer conjugates)
 RN 135649-01-3 HCAPLUS
 CN Poly(oxy-1,2-ethanediyl), .alpha.-[[(2,5-dioxo-1-pyrrolidinyl)oxy]carbonyl]-.omega.-methoxy- (9CI) (CA INDEX NAME)

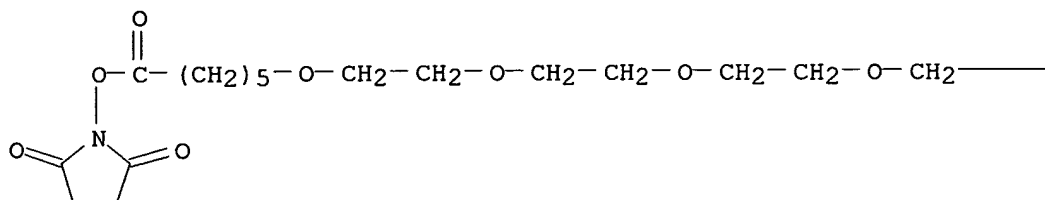


RN 259228-98-3 HCAPLUS
 CN Hexadecanoic acid, 2-[2-[2-[[[(2,5-dioxo-1-pyrrolidinyl)oxy]carbonyl]oxy]ethoxy]ethoxy]ethyl ester (9CI) (CA INDEX NAME)

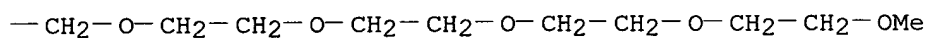


RN 477775-63-6 HCAPLUS
 CN 2,5-Pyrrolidinedione, 1-[(1-oxo-7,10,13,16,19,22,25,28,31-nonaaxadotriacont-1-yl)oxy]- (9CI) (CA INDEX NAME)

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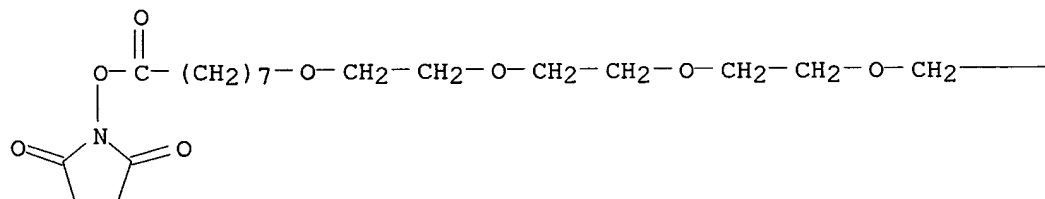


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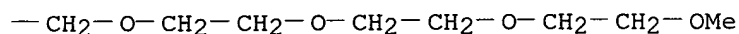


RN 477775-66-9 HCAPLUS
 CN 2,5-Pyrrolidinedione, 1-[(1-oxo-9,12,15,18,21,24,27,30-octaoxahentriacont-1-yl)oxy]- (9CI) (CA INDEX NAME)

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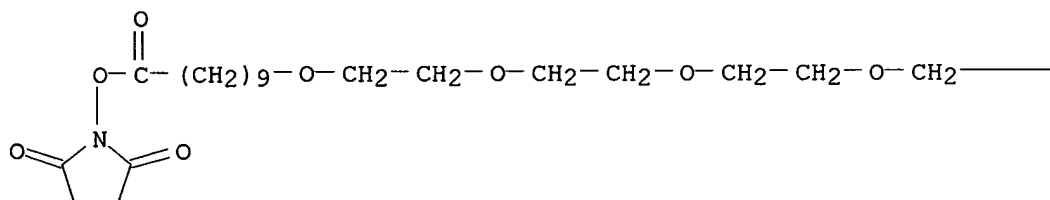


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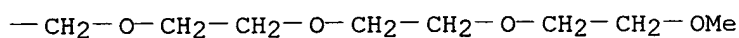


RN 477775-70-5 HCAPLUS
 CN 2,5-Pyrrolidinedione, 1-[(1-oxo-11,14,17,20,23,26,29,32-octaoxatritriacont-1-yl)oxy]- (9CI) (CA INDEX NAME)

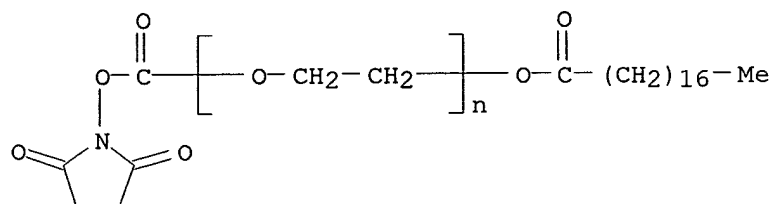
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PAGE 1-B

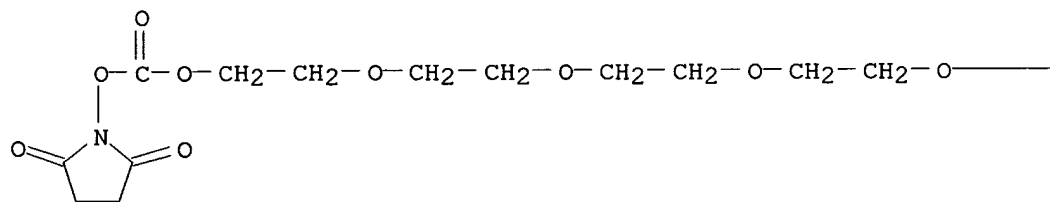


RN 477775-72-7 HCAPLUS
 CN Poly(oxy-1,2-ethanediyl), .alpha.-[[(2,5-dioxo-1-pyrrolidinyl)oxy]carbonyl]-.omega.-[(1-oxooctadecyl)oxy]- (9CI) (CA INDEX NAME)

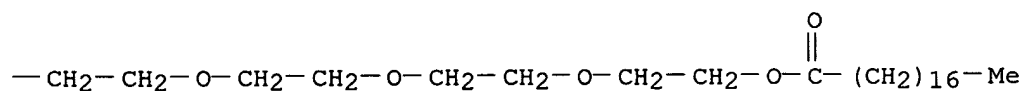


RN 477775-76-1 HCAPLUS
 CN Octadecanoic acid, 25-[(2,5-dioxo-1-pyrrolidinyl)oxy]-25-oxo-3,6,9,12,15,18,21,24-octaioxapentacos-1-yl ester (9CI) (CA INDEX NAME)

PAGE 1-A



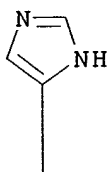
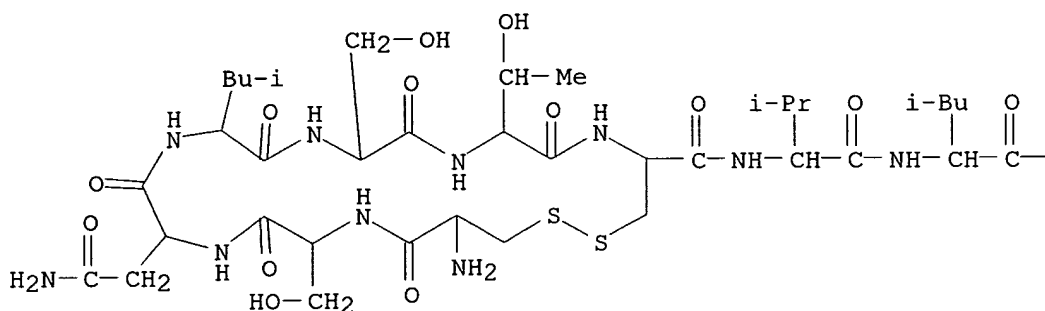
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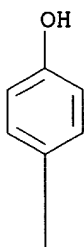
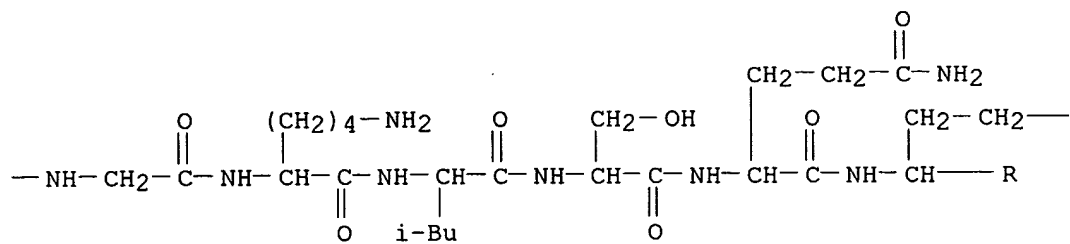
IT 9007-12-9DP, Calcitonin, conjugates with alkylene glycols
 47931-85-1DP, Salmon Calcitonin, conjugates with alkylene glycols
 135649-01-3DP, conjugates with calcitonin 259228-98-3DP,
 conjugates with calcitonin 477775-63-6DP, conjugates with
 calcitonin 477775-66-9DP, conjugates with calcitonin
 477775-70-5DP, conjugates with calcitonin 477775-72-7DP,
 conjugates with calcitonin 477775-76-1DP, conjugates with
 calcitonin 477775-77-2DP, conjugates with calcitonin
 RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
 study); PREP (Preparation); USES (Uses)
 (prepn. of calcitonin drug-alkylene glycol oligomer conjugates)
 RN 9007-12-9 HCAPLUS
 CN Calcitonin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
 RN 47931-85-1 HCAPLUS
 CN Calcitonin (salmon) (8CI, 9CI) (CA INDEX NAME)

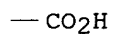
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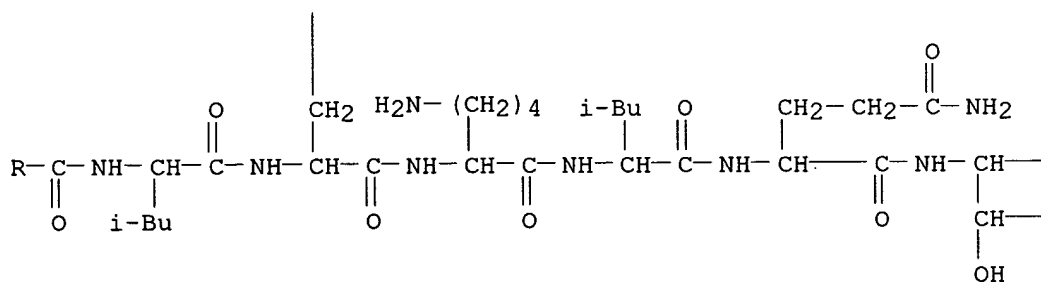
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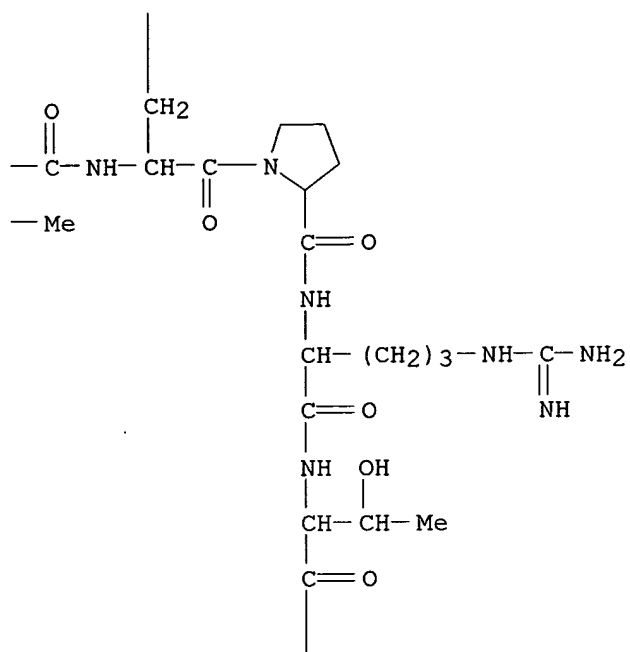
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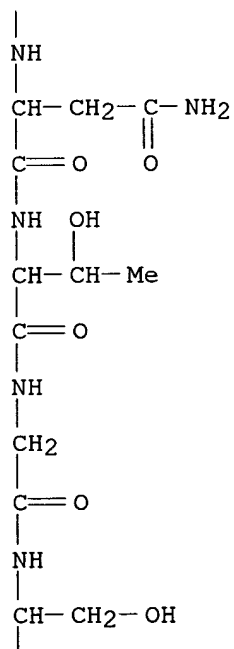
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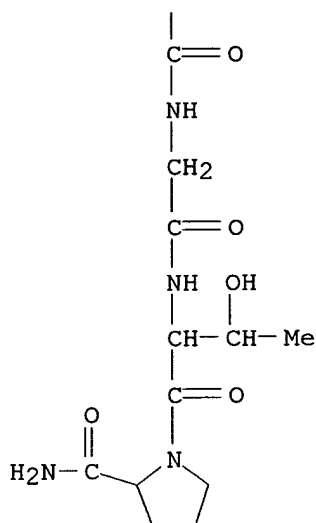
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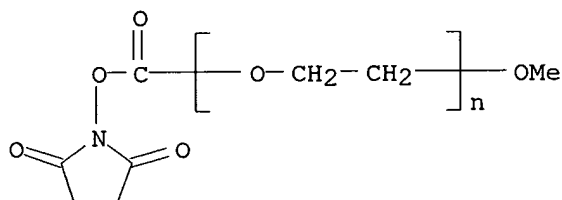
PAGE 3-B



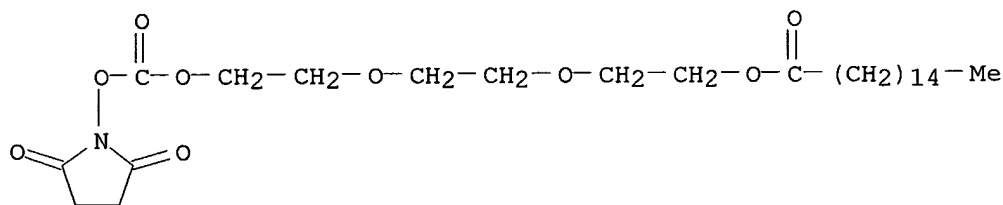
PAGE 4-B



RN 135649-01-3 HCAPLUS
 CN Poly(oxy-1,2-ethanediyl), .alpha.-[[(2,5-dioxo-1-pyrrolidinyloxy)carbonyl]-.omega.-methoxy- (9CI) (CA INDEX NAME)

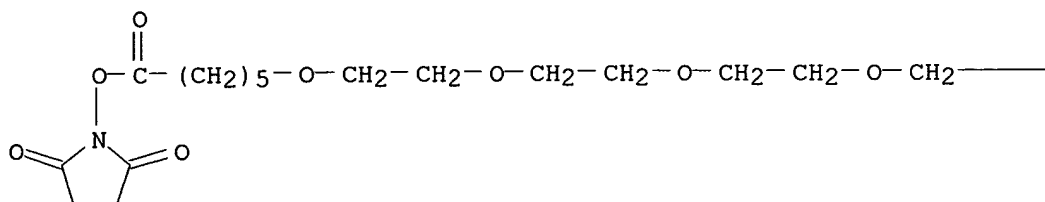


RN 259228-98-3 HCAPLUS
 CN Hexadecanoic acid, 2-[2-[2-[[(2,5-dioxo-1-pyrrolidinyloxy)carbonyl]oxy]ethoxy]ethoxy]ethyl ester (9CI) (CA INDEX NAME)

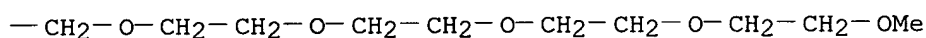


RN 477775-63-6 HCAPLUS
 CN 2,5-Pyrrolidinedione, 1-[(1-oxo-7,10,13,16,19,22,25,28,31-nonaoxadotriacont-1-yl)oxy]- (9CI) (CA INDEX NAME)

PAGE 1-A

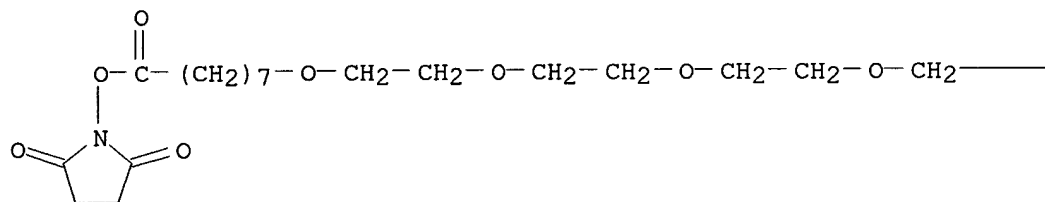


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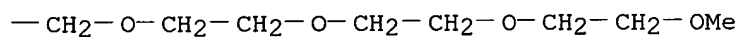


RN 477775-66-9 HCAPLUS
 CN 2,5-Pyrrolidinedione, 1-[(1-oxo-9,12,15,18,21,24,27,30-octaoxahentriacont-1-yl)oxy]-(9CI) (CA INDEX NAME)

PAGE 1-A

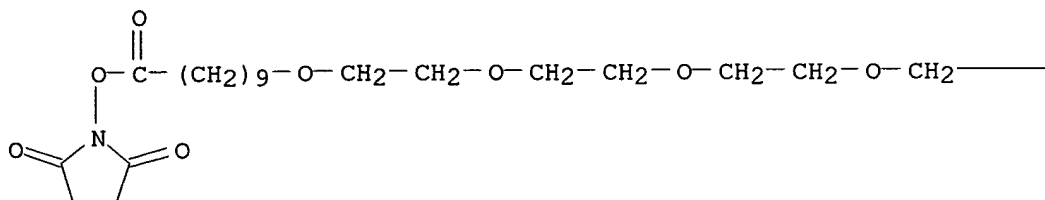


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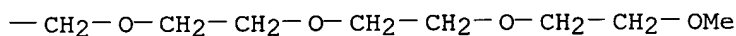


RN 477775-70-5 HCAPLUS
 CN 2,5-Pyrrolidinedione, 1-[(1-oxo-11,14,17,20,23,26,29,32-octaoxatritriacont-1-yl)oxy]-(9CI) (CA INDEX NAME)

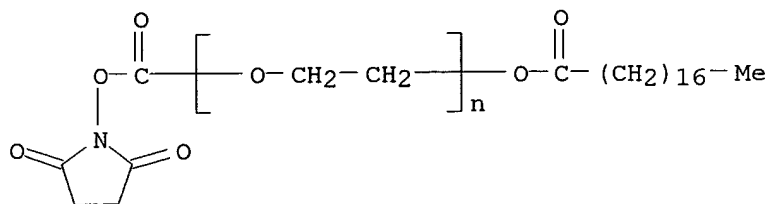
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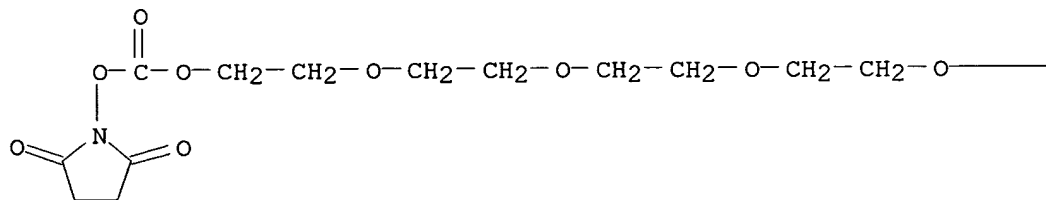


RN 477775-72-7 HCAPLUS
 CN Poly(oxy-1,2-ethanediyl), .alpha.-[[(2,5-dioxo-1-pyrrolidinyl)oxy]carbonyl]-.omega.-[(1-oxooctadecyl)oxy]- (9CI) (CA INDEX NAME)

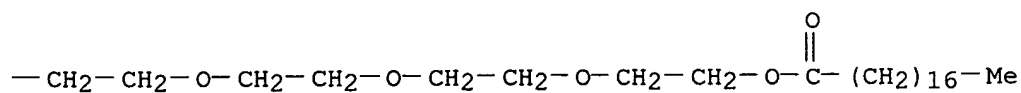


RN 477775-76-1 HCAPLUS
 CN Octadecanoic acid, 25-[(2,5-dioxo-1-pyrrolidinyl)oxy]-25-oxo-3,6,9,12,15,18,21,24-octaoxapentacos-1-yl ester (9CI) (CA INDEX NAME)

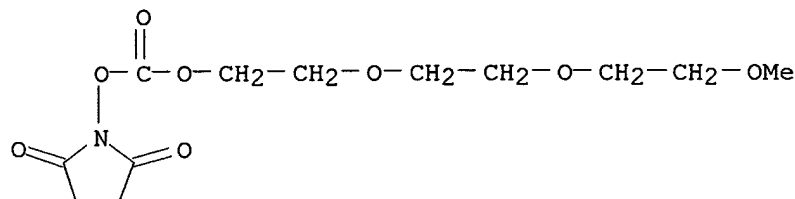
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RN 477775-77-2 HCAPLUS
CN 2,5-Pyrrolidinedione, 1-[(1-oxo-2,5,8,11-tetraoxadodec-1-yl)oxy]- (9CI)
(CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:946130 HCAPLUS
DOCUMENT NUMBER: 138:29120
TITLE: Preparation of peptide drug-alkylene glycol oligomer conjugates
INVENTOR(S): Ekwuribe, Nnochiri N.; Price, Christopher H.; Ansari, Aslam M.; Odenbaugh, Amy L.
PATENT ASSIGNEE(S): Nobex Corporation, USA
SOURCE: PCT Int. Appl., 201 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002098446	A1	20021212	WO 2002-US17567	20020604
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: US 2001-873797 A 20010604

OTHER SOURCE(S): MARPAT 138:29120

AB A non-polydispersed mixt. of conjugates in which each conjugate in the mixt. comprises a peptide drug coupled to an oligomer that includes a polyalkylene glycol moiety is disclosed. The mixt. may exhibit higher in vivo activity than a polydispersed mixt. of similar conjugates. The mixt. may be more effective at surviving an in vitro model of intestinal digestion than polydispersed mixts. of similar conjugates. The mixt. may result in less inter-subject variability than polydispersed mixts. of similar conjugates. Thus, non-polydispersed hexaethylene glycol was treated with phosgene soln., followed by treatment with

N-hydroxysuccinimide (NHS) to give give the NHS ester. Human growth hormone (Saizen) was allowed to react with the NHS ester to give the conjugate.

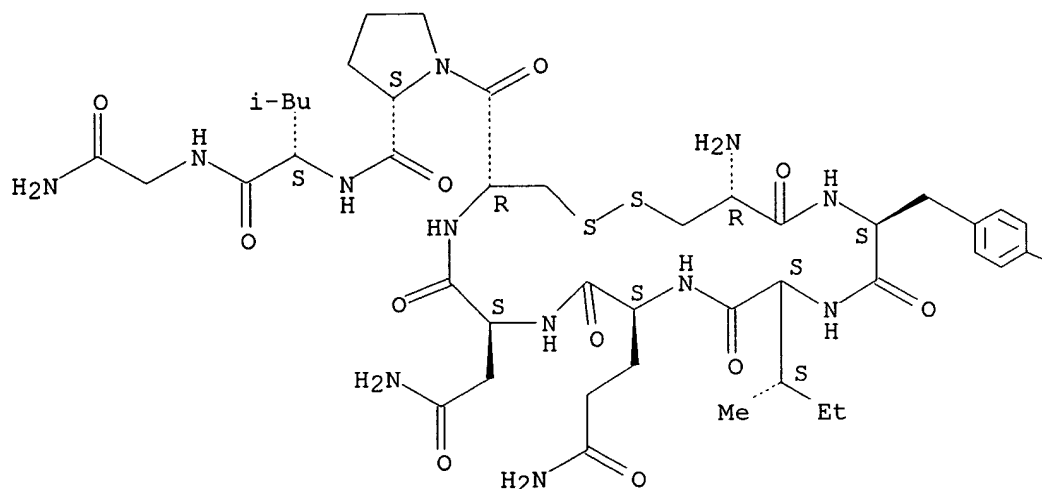
IT 50-56-6DP, Oxytocin, conjugates with alkylene glycols
 1393-25-5DP, Secretin, conjugates with alkylene glycols
 9002-64-6DP, PTH, conjugates with alkylene glycols
 39362-14-6DP, Prolactin-releasing peptide, conjugates with alkylene glycols 82785-45-3DP, Neuropeptide Y, conjugates with alkylene glycols 103370-86-1DP, Parathyroid hormone-related peptide, conjugates with alkylene glycols 106388-42-5DP, Peptide YY, conjugates with alkylene glycols 117148-67-1DP, Pancreastatin, conjugates with alkylene glycols 137061-48-4DP, PACap, conjugates with alkylene glycols 245359-74-4DP, Orexin, conjugates with alkylene glycols
 RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (conjugates with alkylene glycols; prepn. of peptide drug-alkylene glycol oligomer conjugates)

RN 50-56-6 HCAPLUS

CN Oxytocin (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.

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OH

RN 1393-25-5 HCAPLUS
CN Secretin (7CI, 8CI, 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 9002-64-6 HCAPLUS
CN Parathormone (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 39362-14-6 HCAPLUS
CN Prolactin-releasing factor (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 82785-45-3 HCAPLUS
CN Neuropeptide Y (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 103370-86-1 HCAPLUS
CN Humoral hypercalcemic factor (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 106388-42-5 HCAPLUS
CN Peptide YY (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 117148-67-1 HCAPLUS
CN Pancreastatin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 137061-48-4 HCAPLUS
CN Pituitary adenylate cyclase-activating peptide (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 245359-74-4 HCAPLUS
CN Orexin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

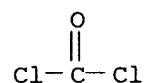
IT 57-10-3, Palmitic acid, reactions 75-44-5, Phosgene
111-77-3 112-27-6, Triethylene glycol 112-35-6
112-76-5, Octadecanoyl chloride 1679-53-4,
10-Hydroxydecanoic acid 2615-15-8 5299-60-5, Ethyl
6-hydroxyhexanoate 6066-82-6, N-Hydroxysuccinimide
25322-68-3, Polyethylene glycol 74124-79-1
RL: RCT (Reactant); RACT (Reactant or reagent)

(in alkylene glycol derivs. prepn.; prepn. of peptide drug-alkylene glycol oligomer conjugates)

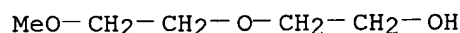
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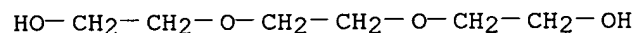
RN 75-44-5 HCAPLUS
CN Carbonic dichloride (9CI) (CA INDEX NAME)



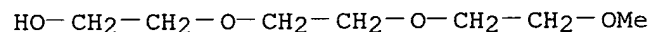
RN 111-77-3 HCAPLUS
CN Ethanol, 2-(2-methoxyethoxy)- (6CI, 8CI, 9CI) (CA INDEX NAME)



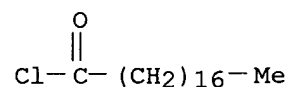
RN 112-27-6 HCAPLUS
CN Ethanol, 2,2'-[1,2-ethanediylbis(oxy)]bis- (9CI) (CA INDEX NAME)



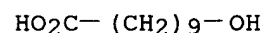
RN 112-35-6 HCAPLUS
CN Ethanol, 2-[2-(2-methoxyethoxy)ethoxy]- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



RN 112-76-5 HCAPLUS
CN Octadecanoyl chloride (9CI) (CA INDEX NAME)

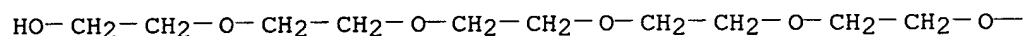


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CN Decanoic acid, 10-hydroxy- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

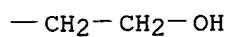


RN 2615-15-8 HCAPLUS
CN 3,6,9,12,15-Pentaoxaheptadecane-1,17-diol (9CI) (CA INDEX NAME)

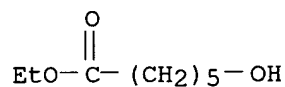
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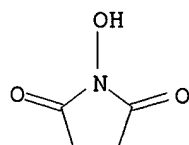
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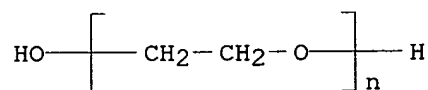
RN 5299-60-5 HCAPLUS
CN Hexanoic acid, 6-hydroxy-, ethyl ester (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



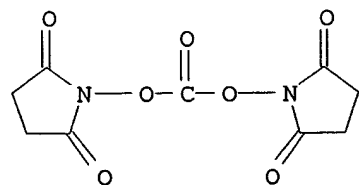
RN 6066-82-6 HCAPLUS
CN 2,5-Pyrrolidinedione, 1-hydroxy- (9CI) (CA INDEX NAME)



RN 25322-68-3 HCAPLUS
CN Poly(oxy-1,2-ethanediyl), .alpha.-hydro-.omega.-hydroxy- (9CI) (CA INDEX NAME)



RN 74124-79-1 HCAPLUS
CN 2,5-Pyrrolidinedione, 1,1'-[carbonylbis(oxy)]bis- (9CI) (CA INDEX NAME)

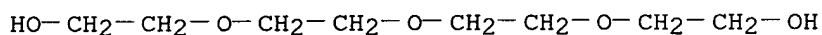


IT 112-60-7P, Tetraethylene glycol 3639-35-8P

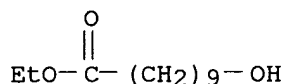
4437-01-8P, 2,5,8,11,14,17,20-Heptaoxidocosan-22-ol
 9004-74-4P 9004-99-3P 17696-11-6P
 24342-68-5P 29823-21-0P 62304-85-2P
 70802-40-3P 74654-05-0P 86259-87-2P
 105292-71-5P 124668-93-5P 142556-85-2P
 175172-61-9P 477775-58-9P 477775-59-0P
 477775-60-3P 477775-61-4P 477775-62-5P
 477775-65-8P 477775-67-0P 477775-68-1P
 477775-69-2P 477775-71-6P 477775-73-8P
 477775-74-9P 477775-75-0P 477781-68-3P
 477781-69-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)
 (in alkylene glycol derivs. prepn.; prepn. of peptide drug-alkylene
 glycol oligomer conjugates)

RN 112-60-7 HCAPLUS
 CN Ethanol, 2,2'-[oxybis(2,1-ethanediyl oxy)]bis- (9CI) (CA INDEX NAME)

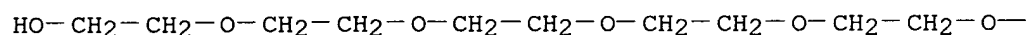


RN 3639-35-8 HCAPLUS
 CN Decanoic acid, 10-hydroxy-, ethyl ester (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

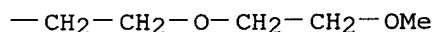


RN 4437-01-8 HCAPLUS
 CN 2,5,8,11,14,17,20-Heptaoxidocosan-22-ol (6CI, 8CI, 9CI) (CA INDEX NAME)

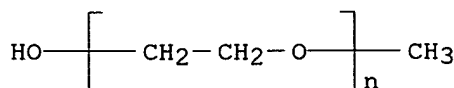
PAGE 1-A



PAGE 1-B

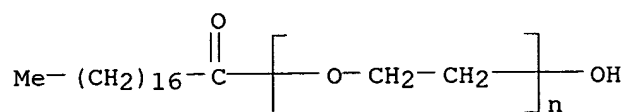


RN 9004-74-4 HCAPLUS
 CN Poly(oxy-1,2-ethanediyl), .alpha.-methyl-.omega.-hydroxy- (9CI) (CA INDEX NAME)



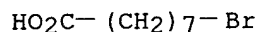
RN 9004-99-3 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), .alpha.-(1-oxooctadecyl)-.omega.-hydroxy- (9CI)
(CA INDEX NAME)



RN 17696-11-6 HCAPLUS

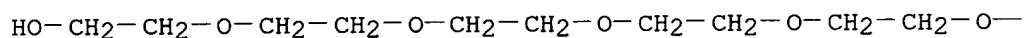
CN Octanoic acid, 8-bromo- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



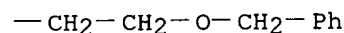
RN 24342-68-5 HCAPLUS

CN 2,5,8,11,14,17-Hexaoxonadecan-19-ol, 1-phenyl- (9CI) (CA INDEX NAME)

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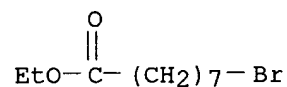


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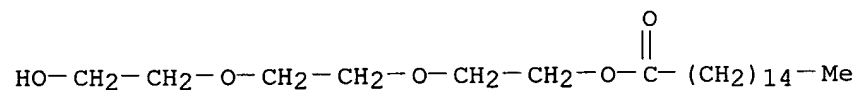
RN 29823-21-0 HCAPLUS

CN Octanoic acid, 8-bromo-, ethyl ester (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



RN 62304-85-2 HCAPLUS

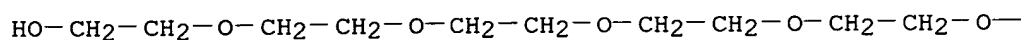
CN Hexadecanoic acid, 2-[2-(2-hydroxyethoxy)ethoxy]ethyl ester (9CI) (CA INDEX NAME)



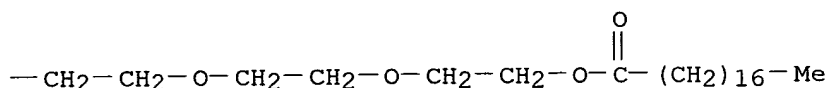
RN 70802-40-3 HCAPLUS

CN Octadecanoic acid, 23-hydroxy-3,6,9,12,15,18,21-heptaotricos-1-yl ester (9CI) (CA INDEX NAME)

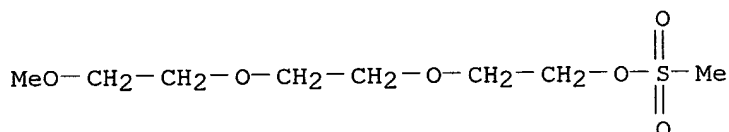
PAGE 1-A



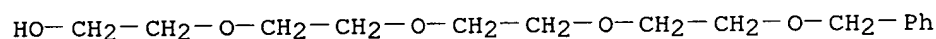
PAGE 1-B



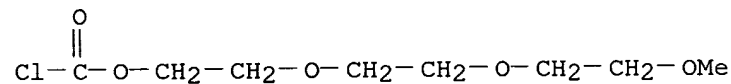
RN 74654-05-0 HCAPLUS
CN Ethanol, 2-[2-(2-methoxyethoxy)ethoxy]-, methanesulfonate (9CI) (CA INDEX NAME)



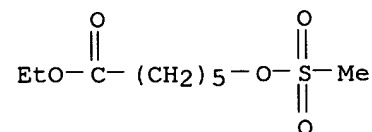
RN 86259-87-2 HCAPLUS
CN 2,5,8,11-Tetraoxatridecan-13-ol, 1-phenyl- (9CI) (CA INDEX NAME)



RN 105292-71-5 HCAPLUS
CN Carbonochloridic acid, 2-[2-(2-methoxyethoxy)ethoxy]ethyl ester (9CI) (CA INDEX NAME)



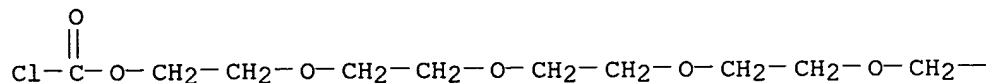
RN 124668-93-5 HCAPLUS
CN Hexanoic acid, 6-[(methylsulfonyl)oxy]-, ethyl ester (9CI) (CA INDEX NAME)



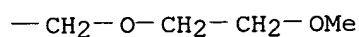
RN 142556-85-2 HCAPLUS

CN Carbonochloridic acid, 3,6,9,12,15,18-hexaoxonadec-1-yl ester (9CI) (CA INDEX NAME)

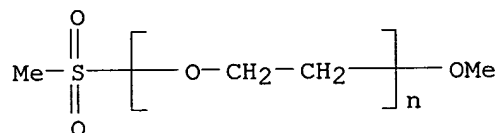
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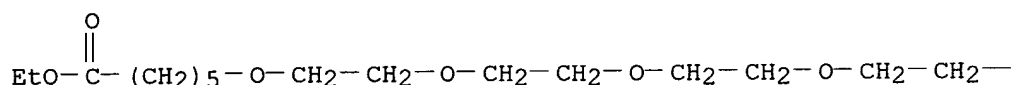


RN 175172-61-9 HCAPLUS
CN Poly(oxy-1,2-ethanediyl), .alpha.-(methylsulfonyl)-.omega.-methoxy- (9CI)
(CA INDEX NAME)

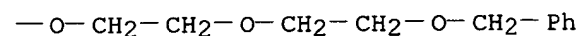


RN 477775-58-9 HCAPLUS
CN 2,5,8,11,14,17,20-Heptaohaxacosan-26-oic acid, 1-phenyl-, ethyl ester
(9CI) (CA INDEX NAME)

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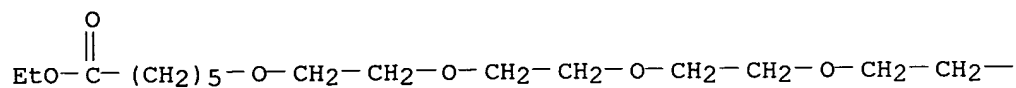


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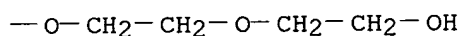


RN 477775-59-0 HCAPLUS
CN 3,6,9,12,15,18-Hexaoxatetracosan-24-oic acid, 1-hydroxy-, ethyl ester
(9CI) (CA INDEX NAME)

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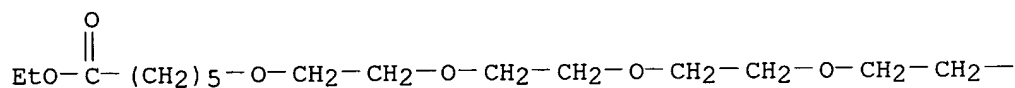


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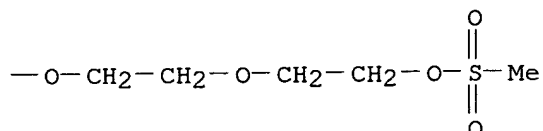


RN 477775-60-3 HCAPLUS
CN 3,6,9,12,15,18-Hexaoxatetracosan-24-oic acid, 1-[(methylsulfonyl)oxy]-,
ethyl ester (9CI) (CA INDEX NAME)

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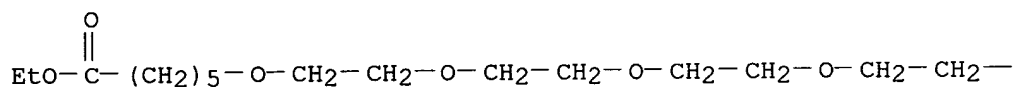


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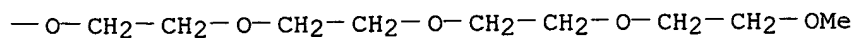


RN 477775-61-4 HCAPLUS
CN 2,5,8,11,14,17,20,23,26-Nonaoxadotriacontan-32-oic acid, ethyl ester (9CI)
(CA INDEX NAME)

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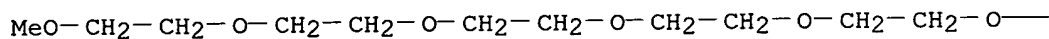
PAGE 1-B



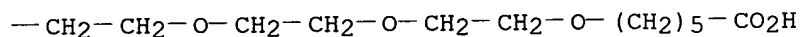
RN 477775-62-5 HCAPLUS

CN 2,5,8,11,14,17,20,23,26-Nonaoxadotriacontan-32-oic acid (9CI) (CA INDEX NAME)

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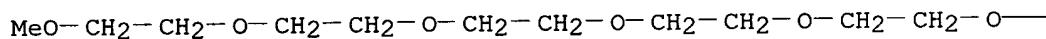


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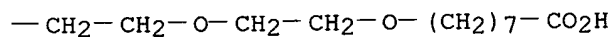


RN 477775-65-8 HCAPLUS
CN 2,5,8,11,14,17,20,23-Octaoxahentriacontan-31-oic acid (9CI) (CA INDEX NAME)

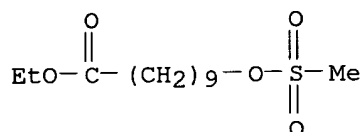
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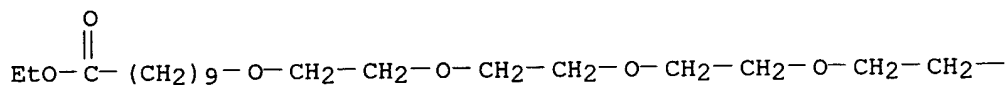


RN 477775-67-0 HCAPLUS
CN Decanoic acid, 10-[(methylsulfonyl)oxy]-, ethyl ester (9CI) (CA INDEX NAME)

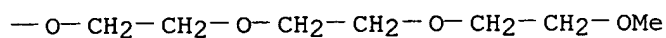


RN 477775-68-1 HCAPLUS
CN 2,5,8,11,14,17,20,23-Octaoxatritriacontan-33-oic acid, ethyl ester (9CI) (CA INDEX NAME)

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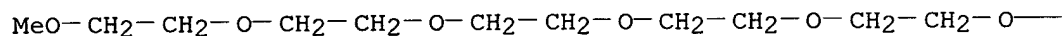


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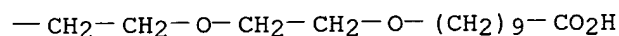


RN 477775-69-2 HCAPLUS
CN 2,5,8,11,14,17,20,23-Octaoxatritriacontan-33-oic acid (9CI) (CA INDEX NAME)

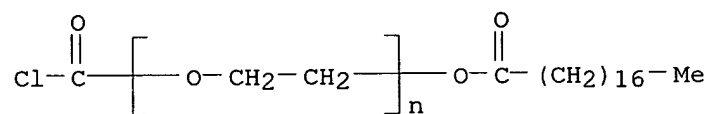
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PAGE 1-B

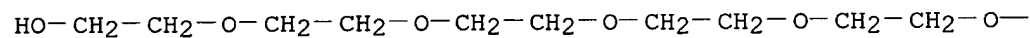


RN 477775-71-6 HCAPLUS
CN Poly(oxy-1,2-ethanediyl), .alpha.-(chlorocarbonyl)-.omega.-[(1-oxooctadecyl)oxy]- (9CI) (CA INDEX NAME)

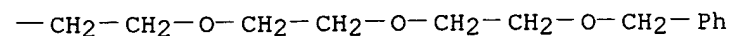


RN 477775-73-8 HCAPLUS
CN 2,5,8,11,14,17,20,23-Octaoxapentacosan-25-ol, 1-phenyl- (9CI) (CA INDEX NAME)

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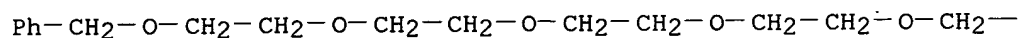


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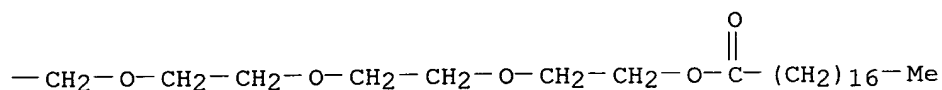


RN 477775-74-9 HCAPLUS
CN Octadecanoic acid, 25-phenyl-3,6,9,12,15,18,21,24-octaoxapentacos-1-yl ester (9CI) (CA INDEX NAME)

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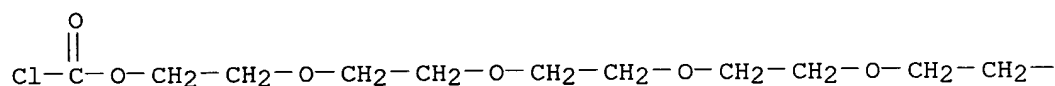


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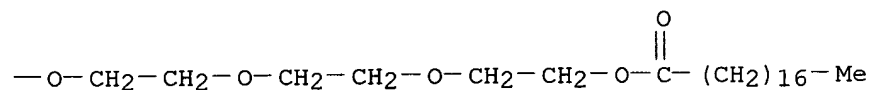


RN 477775-75-0 HCAPLUS
CN Octadecanoic acid, 25-chloro-25-oxo-3,6,9,12,15,18,21,24-octaoxapentacos-1-yl ester (9CI) (CA INDEX NAME)

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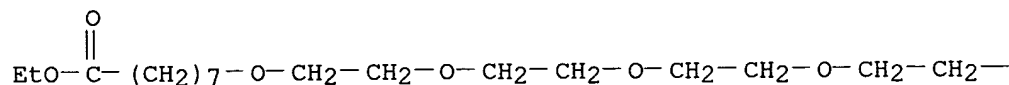


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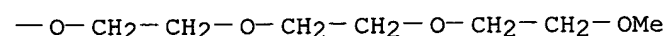


RN 477781-68-3 HCAPLUS
CN 2,5,8,11,14,17,20,23-Octaoxahentriacontan-31-oic acid, ethyl ester (9CI)
(CA INDEX NAME)

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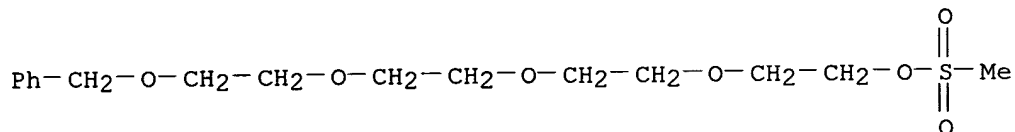


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RN 477781-69-4 HCAPLUS
CN 2,5,8,11-Tetraoxatridecan-13-ol, 1-phenyl-, methanesulfonate (9CI) (CA

INDEX NAME)

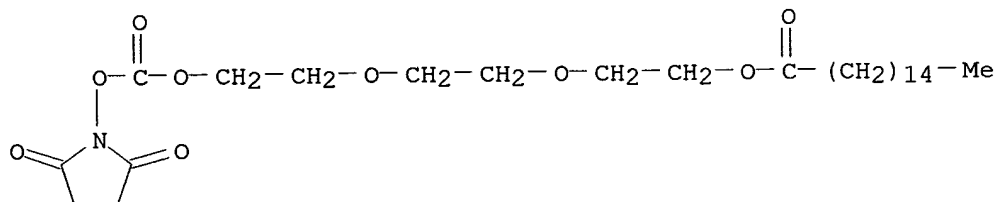


IT 259228-98-3P 477775-63-6P 477775-66-9P
477775-70-5P 477775-72-7P 477775-76-1P
477775-77-2P 477788-13-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(prepn. of peptide drug-alkylene glycol oligomer conjugates)

RN 259228-98-3 HCAPLUS

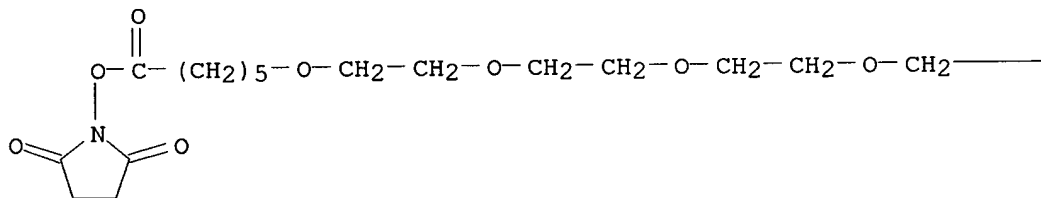
CN Hexadecanoic acid, 2-[2-[2-[[[(2,5-dioxo-1-pyrrolidinyl)oxy]carbonyl]oxy]e
thoxy]ethoxy]ethyl ester (9CI) (CA INDEX NAME)



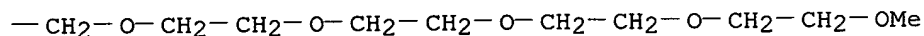
RN 477775-63-6 HCAPLUS

CN 2,5-Pyrrolidinedione, 1-[(1-oxo-7,10,13,16,19,22,25,28,31-
nonaoxadotriacont-1-yl)oxy]- (9CI) (CA INDEX NAME)

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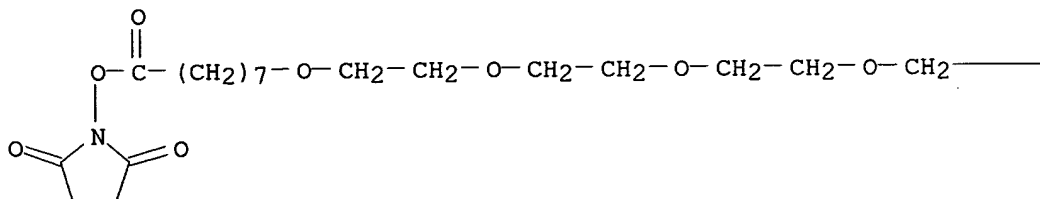
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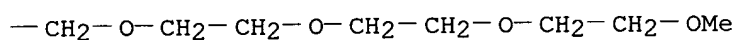
RN 477775-66-9 HCAPLUS

CN 2,5-Pyrrolidinedione, 1-[(1-oxo-9,12,15,18,21,24,27,30-octaoxahentriacont-
1-yl)oxy]- (9CI) (CA INDEX NAME)

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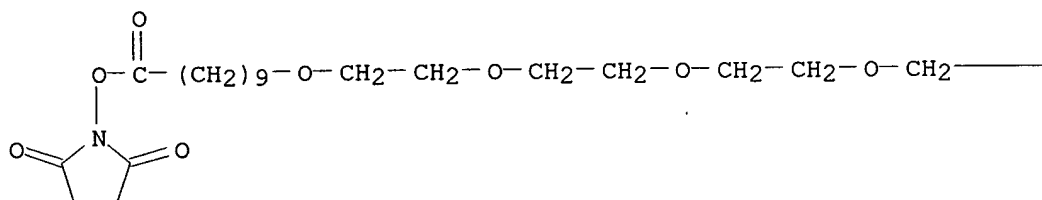


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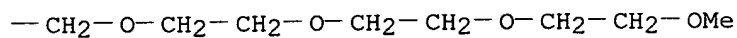


RN 477775-70-5 HCAPLUS
 CN 2,5-Pyrrolidinedione, 1-[(1-oxo-11,14,17,20,23,26,29,32-octaoxatritriacont-1-yl)oxy]-(9CI) (CA INDEX NAME)

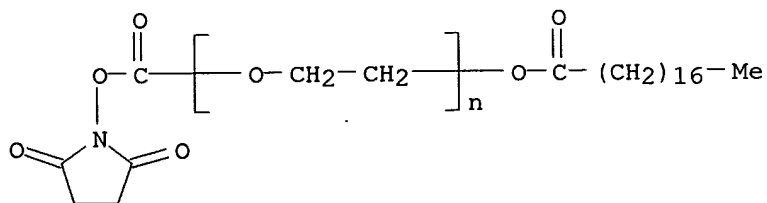
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PAGE 1-B

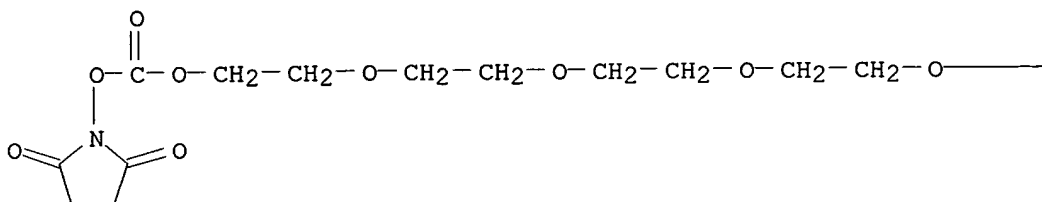


RN 477775-72-7 HCAPLUS
 CN Poly(oxy-1,2-ethanediyl), .alpha.-[[(2,5-dioxo-1-pyrrolidinyl)oxy]carbonyl]-.omega.-[(1-oxooctadecyl)oxy]-(9CI) (CA INDEX NAME)

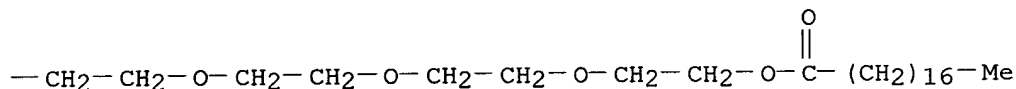


RN 477775-76-1 HCAPLUS
 CN Octadecanoic acid, 25-[(2,5-dioxo-1-pyrrolidinyl)oxy]-25-oxo-
 3,6,9,12,15,18,21,24-octaoxapentacos-1-yl ester (9CI) (CA INDEX NAME)

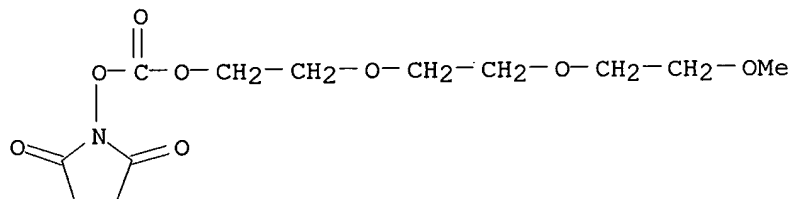
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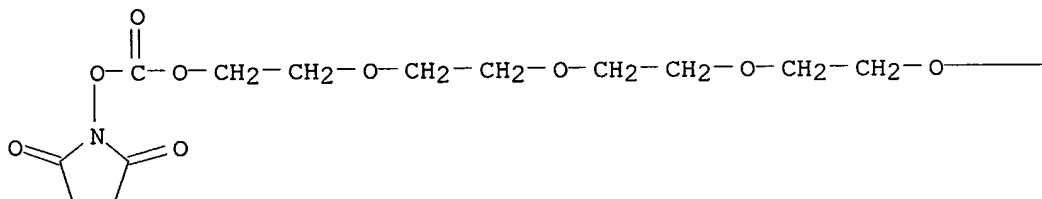


RN 477775-77-2 HCAPLUS
 CN 2,5-Pyrrolidinedione, 1-[(1-oxo-2,5,8,11-tetraoxadodec-1-yl)oxy]- (9CI)
 (CA INDEX NAME)



RN 477788-13-9 HCAPLUS
 CN 2,5-Pyrrolidinedione, 1-[(1-oxo-2,5,8,11,14,17,20-heptaoxaheneicos-1-yl)oxy]- (9CI) (CA INDEX NAME)

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— CH₂—CH₂—O—CH₂—CH₂—OMe

IT 58-82-2DP, Bradykinin, conjugates with alkylene glycols
 1407-47-2DP, Angiotensin, conjugates with alkylene glycols
 8049-62-5DP, Zinc insulin, conjugates with alkylene glycols
 9002-60-2DP, ACTH, conjugates with alkylene glycols
 9002-76-0DP, Gastrin, conjugates with alkylene glycols
 9002-79-3DP, Melanocyte stimulating hormone, conjugates with
 alkylene glycols 9004-10-8DP, Insulin, conjugates with alkylene
 glycols 9007-92-5DP, Glucagon, conjugates with alkylene glycols
 9011-97-6DP, Cholecystokinin, conjugates with alkylene glycols
 9015-71-8DP, Corticotropin releasing factor, conjugates with
 alkylene glycols 9015-94-5DP, Renin, conjugates with alkylene
 glycols 9034-40-6DP, LHRH, conjugates with alkylene glycols
 11000-17-2DP, Vasopressin, conjugates with alkylene glycols
 11061-68-0DP, Human insulin, conjugates with alkylene glycols
 12629-01-5DP, Human growth hormone, conjugates with alkylene
 glycols 24305-27-9DP, Thyrotropin-releasing hormone, conjugates
 with alkylene glycols 31362-50-2DP, Bombesin, conjugates with
 alkylene glycols 33507-63-0DP, Substance P, conjugates with
 alkylene glycols 37221-79-7DP, Vasoactiveintestinal peptide,
 conjugates with alkylene glycols 47931-85-1DP, Salmon
 calcitonin, conjugates with alkylene glycols 51110-01-1DP,
 Somatostatin, conjugates with alkylene glycols 52906-92-0DP,
 Motilin, conjugates with alkylene glycols 57285-09-3DP, Inhibin,
 conjugates with alkylene glycols 58391-28-9DP, Leucokinin,
 conjugates with alkylene glycols 59112-80-0DP, C-Peptide,
 conjugates with alkylene glycols 60118-07-2DP, Endorphin,
 conjugates with alkylene glycols 72093-21-1DP, Mastoparan,
 conjugates with alkylene glycols 74135-04-9DP, Morphiceptin,
 conjugates with alkylene glycols 74913-18-1DP, Dynorphin,
 conjugates with alkylene glycols 77614-16-5DP, Dermorphin,
 conjugates with alkylene glycols 83652-28-2DP, Calcitonin gene
 related peptide, conjugates with alkylene glycols 83856-13-7DP,
 Mast cell degranulating peptide, conjugates with alkylene glycols
 85568-32-7DP, Casomorphin, conjugates with alkylene glycols
 85637-73-6DP, Atrial natriuretic peptide, conjugates with alkylene
 glycols 106602-62-4DP, Amylin, conjugates with alkylene glycols
 107666-54-6DP, GNRH associated peptide, conjugates with alkylene
 glycols 110119-33-0DP, Allatostatin, conjugates with alkylene
 glycols 114471-18-0DP, Brain natriuretic peptide, conjugates
 with alkylene glycols 116243-73-3DP, Endothelin, conjugates with
 alkylene glycols 119418-04-1DP, Galanin, conjugates with
 alkylene glycols 127830-04-0DP, C-Type natriuretic peptide,
 conjugates with alkylene glycols 144940-98-7DP, Guanylin,
 conjugates with alkylene glycols 154835-90-2DP, Adrenomedullin,
 conjugates with alkylene glycols 169494-85-3DP, Leptin,
 conjugates with alkylene glycols 193829-96-8DP, Cortistatin,
 conjugates with alkylene glycols 259228-98-3DP, peptide drug
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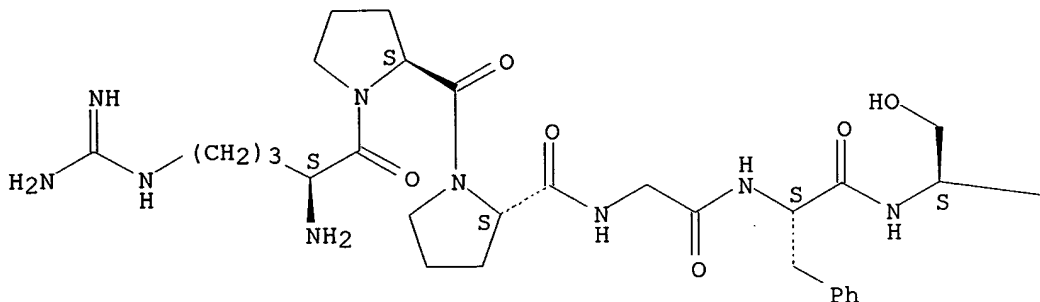
477775-76-1DP, peptide drug conjugates 477775-77-2DP,
 peptide drug conjugates 477788-13-9DP, peptide drug conjugates
 RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
 study); PREP (Preparation); USES (Uses)
 (prepn. of peptide drug-alkylene glycol oligomer conjugates)

RN 58-82-2 HCAPLUS

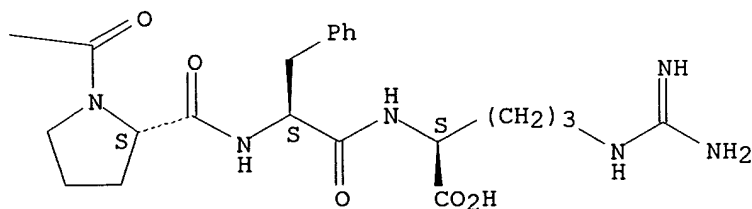
CN Bradykinin (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.

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RN 1407-47-2 HCAPLUS

CN Angiotensin (8CI, 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 8049-62-5 HCAPLUS

CN Insulin zinc (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 9002-60-2 HCAPLUS

CN Corticotropin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 9002-76-0 HCAPLUS

CN Gastrin (hormone) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 9002-79-3 HCAPLUS

CN Melanotropin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 9004-10-8 HCAPLUS

CN Insulin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 9007-92-5 HCAPLUS

CN Glucagon (7CI, 8CI, 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 9011-97-6 HCAPLUS

CN Cholecystokinin (8CI, 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 9015-71-8 HCAPLUS

CN Corticotropin-releasing factor (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 9015-94-5 HCAPLUS

CN Renin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 9034-40-6 HCAPLUS

CN Luteinizing hormone-releasing factor (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 11000-17-2 HCAPLUS

CN Vasopressin (7CI, 8CI, 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 11061-68-0 HCAPLUS

CN Insulin (human) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 12629-01-5 HCAPLUS

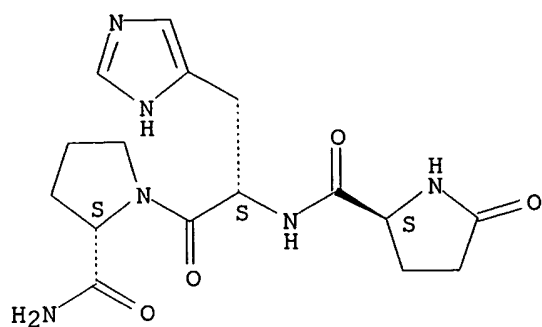
CN Somatotropin (human) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 24305-27-9 HCAPLUS

CN L-Prolinamide, 5-oxo-L-prolyl-L-histidyl- (9CI) (CA INDEX NAME)

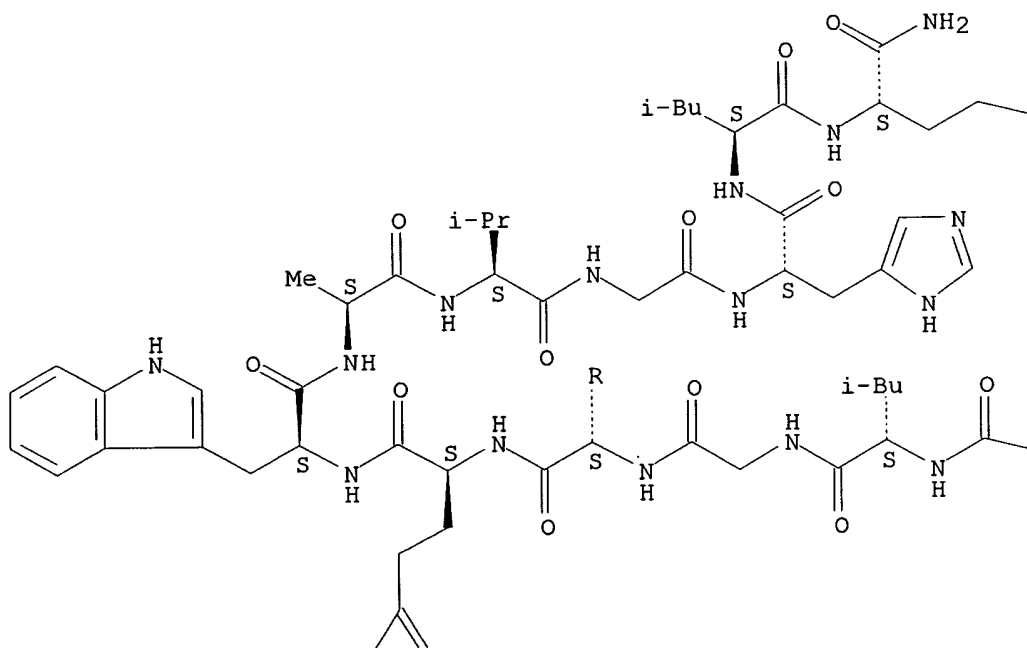
Absolute stereochemistry.



RN 31362-50-2 HCAPLUS
CN Bombesin (9CI) (CA INDEX NAME)

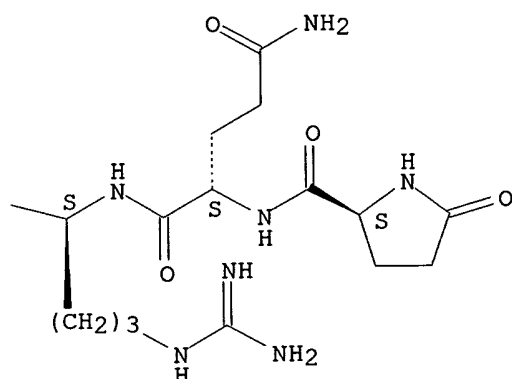
Absolute stereochemistry.

PAGE 1-A

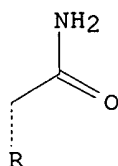
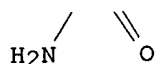


PAGE 1-B

— SMe



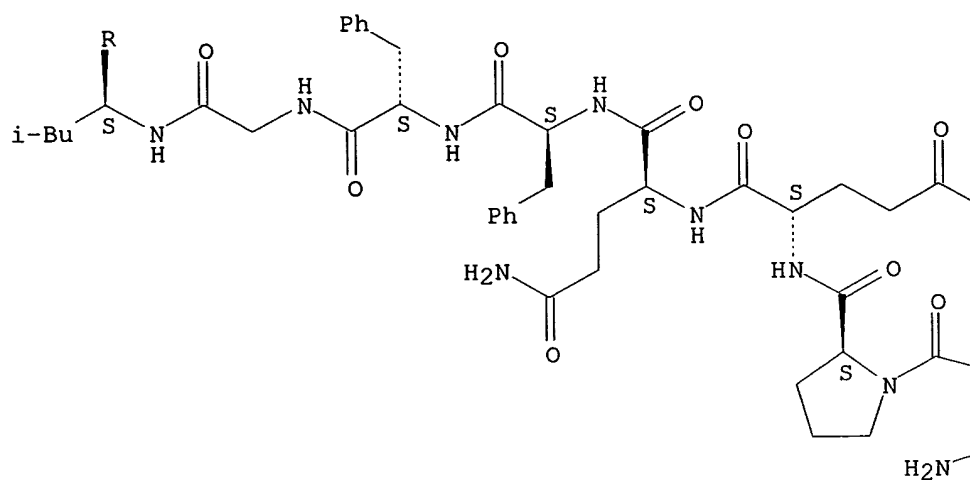
PAGE 2-A



RN 33507-63-0 HCAPLUS
CN Substance P (9CI) (CA INDEX NAME)

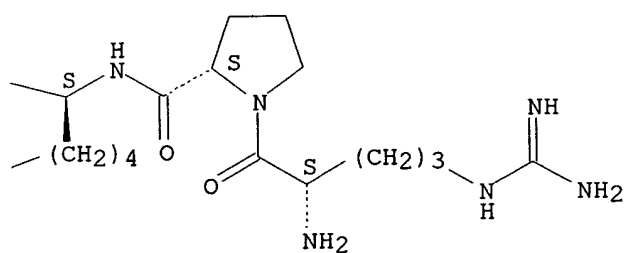
Absolute stereochemistry.

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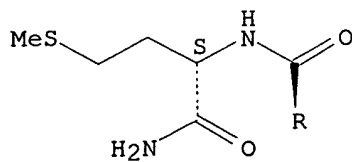


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NH₂



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RN 37221-79-7 HCAPLUS

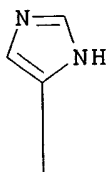
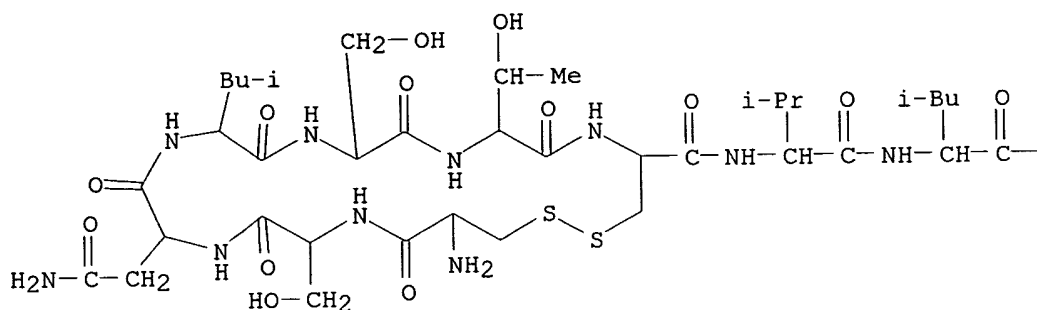
CN Vasoactive intestinal polypeptide (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

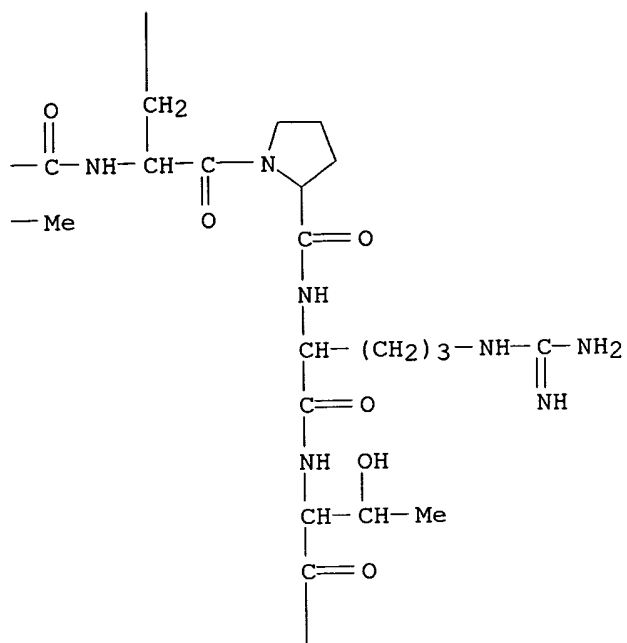
RN 47931-85-1 HCAPLUS

CN Calcitonin (salmon) (8CI, 9CI) (CA INDEX NAME)

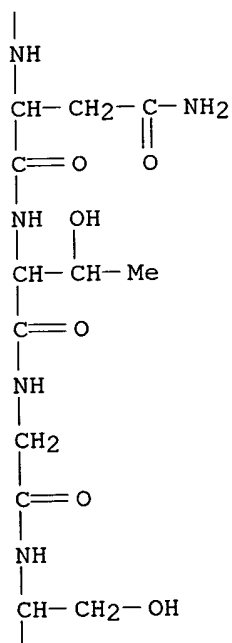
PAGE 1-A



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PAGE 3-B



$$\begin{array}{c}
 | \\
 \text{C}=\text{O} \\
 | \\
 \text{NH} \\
 | \\
 \text{CH}_2 \\
 | \\
 \text{C}=\text{O} \\
 | \\
 \text{NH} \quad \text{OH} \\
 | \quad | \\
 \text{CH}-\text{CH}-\text{Me} \\
 | \\
 \text{C}=\text{O} \\
 | \\
 \text{N} \\
 | \\
 \text{C}=\text{O} \\
 | \\
 \text{H}_2\text{N}
 \end{array}$$

```

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN      72093-21-1  HCAPLUS
CN      Mast cell degranulating peptide (Vespula lewisii) (9CI)  (CA INDEX NAME)

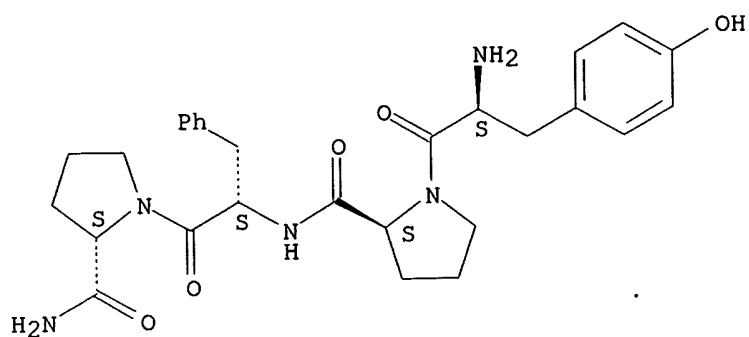
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Chemical structure of the repeating unit of poly(1,3-bis(2-ethyl-2-methyl-1,3-dithiolane-5-carbonyl)-4-aminobutane). The structure shows a chain of amide bonds connecting various thiolane rings. The thiolane rings are substituted with ethyl (Et), methyl (Me), isobutyl (i-Bu), and a 4-aminobutyl group (H₂N-(CH₂)₄-). Stereochemistry is indicated with wedges and dashes.

Chemical structure 10 is a complex thiol derivative. It features a central chain with multiple thiol (-SH) and thioether (-S-) groups. The structure includes a long alkyl chain (CH₂)₄, a methyl group (Me), and a butyl group (Bu-i). The stereochemistry is indicated with wedges and dashes.

Absolute stereochemistry.



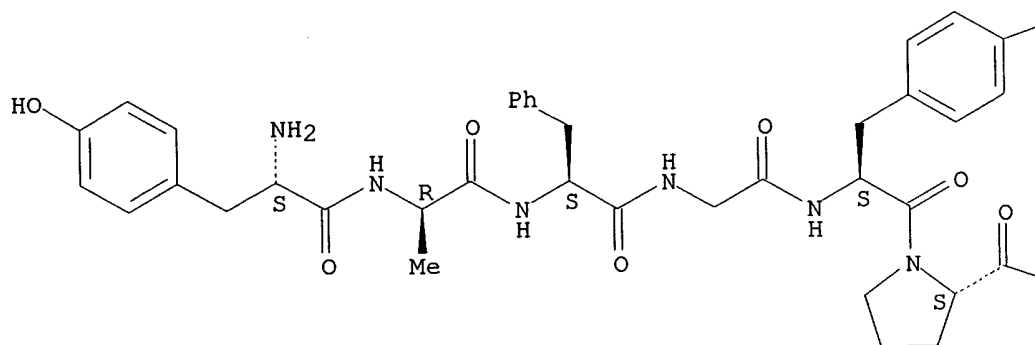
RN 74913-18-1 HCAPLUS
CN Dynorphin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 77614-16-5 HCAPLUS
CN Dermorphin (9CI) (CA INDEX NAME)

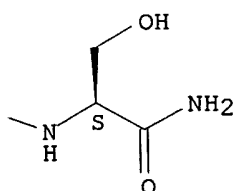
Absolute stereochemistry.

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—OH



RN 83652-28-2 HCAPLUS
 CN Calcitonin gene-related peptide (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
 RN 83856-13-7 HCAPLUS
 CN Mast cell degranulating peptide (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
 RN 85568-32-7 HCAPLUS
 CN Casomorphin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
 RN 85637-73-6 HCAPLUS
 CN Atrial natriuretic peptide (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
 RN 106602-62-4 HCAPLUS
 CN Amylin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
 RN 107666-54-6 HCAPLUS
 CN Luteinizing hormone-releasing factor-associated peptide (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
 RN 110119-33-0 HCAPLUS
 CN Allatostatin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
 RN 114471-18-0 HCAPLUS
 CN Brain natriuretic peptide (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
 RN 116243-73-3 HCAPLUS
 CN Endothelin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
 RN 119418-04-1 HCAPLUS
 CN Galanin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
 RN 127830-04-0 HCAPLUS
 CN C-type natriuretic peptide (9CI) (CA INDEX NAME)

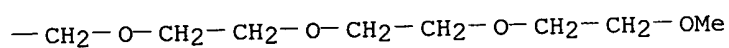
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 CN Guanylin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
 RN 154835-90-2 HCAPLUS
 CN Adrenomedullin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
 RN 169494-85-3 HCAPLUS
 CN Leptin (9CI) (CA INDEX NAME)

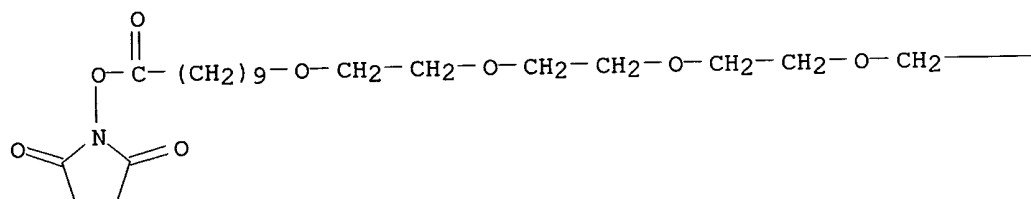
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 RN 193829-96-8 HCAPLUS

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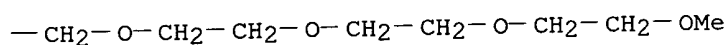


RN 477775-70-5 HCAPLUS
CN 2,5-Pyrrolidinedione, 1-[(1-oxo-11,14,17,20,23,26,29,32-octaoxatritriacont-1-yl)oxy]- (9CI) (CA INDEX NAME)

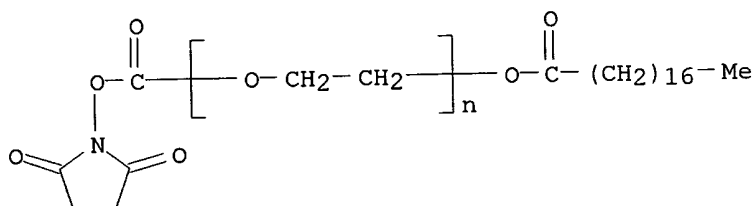
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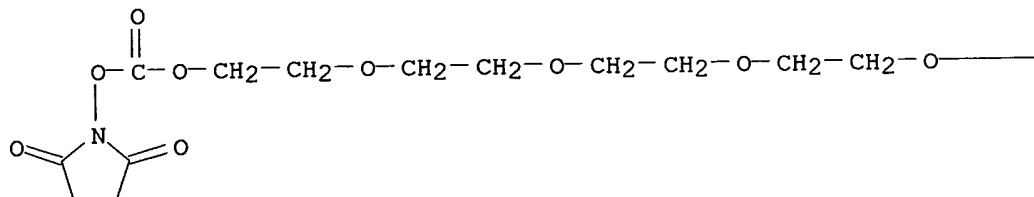


RN 477775-72-7 HCAPLUS
CN Poly(oxy-1,2-ethanediyl), .alpha.-[[(2,5-dioxo-1-pyrrolidinyl)oxy]carbonyl]-.omega.-[(1-oxooctadecyl)oxy]- (9CI) (CA INDEX NAME)

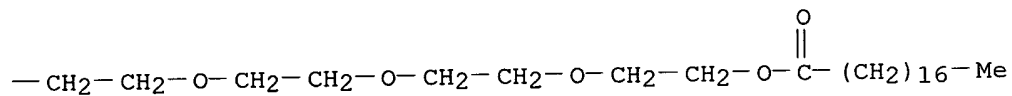


RN 477775-76-1 HCAPLUS
CN Octadecanoic acid, 25-[(2,5-dioxo-1-pyrrolidinyl)oxy]-25-oxo-3,6,9,12,15,18,21,24-octaoxapentacos-1-yl ester (9CI) (CA INDEX NAME)

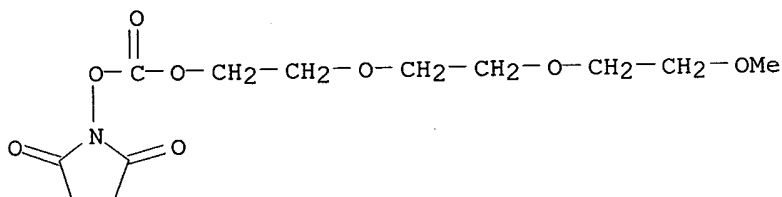
PAGE 1-A



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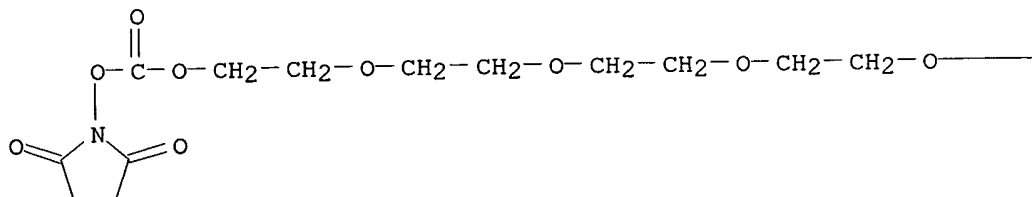


RN 477775-77-2 HCAPLUS
 CN 2,5-Pyrrolidinedione, 1-[(1-oxo-2,5,8,11-tetraoxadodec-1-yl)oxy]- (9CI)
 (CA INDEX NAME)

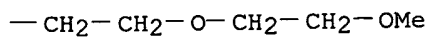


RN 477788-13-9 HCAPLUS
 CN 2,5-Pyrrolidinedione, 1-[(1-oxo-2,5,8,11,14,17,20-heptaoheneicos-1-yl)oxy]- (9CI) (CA INDEX NAME)

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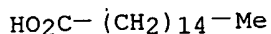
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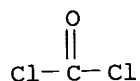
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L7 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2003 ACS
 ACCESSION NUMBER: 2002:946037 HCAPLUS
 DOCUMENT NUMBER: 138:16621
 TITLE: Preparation of insulin-alkylene glycol oligomer conjugates
 INVENTOR(S): Ekwuribe, Nnochiri N.; Price, Christopher H.; Ansari, Aslam M.; Odenbaugh, Amy L.; Radhakrishnan, Balasingam
 PATENT ASSIGNEE(S): Nobex Corporation, USA
 SOURCE: PCT Int. Appl., 127 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

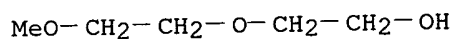
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US 2003027748	A1	20030206	US 2001-873899	20010604
PRIORITY APPLN. INFO.:			US 2001-873899	A 20010604
OTHER SOURCE(S): MARPAT 138:16621				
AB	A mixt. of conjugates in which each conjugate in the mixt. comprises an insulin drug coupled to an oligomer that includes a polyalkylene glycol moiety is disclosed. The mixt. may exhibit higher in vivo activity than a polydispersed mixt. of similar conjugates. The mixt. may also be more effective at surviving an in vitro model of intestinal digestion than polydispersed mixts. of similar conjugates. The mixt. may also result in less inter-subject variability than polydispersed mixts. of similar conjugates. Thus, non-polydispersed hexaethylene glycol was treated with phosgene soln., followed by treatment with N-hydroxysuccinimide (NHS) to give give the NHS ester. Human insulin was dissolved in DMSO and allowed to react with the NHS ester to give the conjugate.			
IT	57-10-3, Palmitic acid, reactions 75-44-5, Phosgene 111-77-3 112-35-6 112-60-7, Tetraethylene glycol 112-76-5, Octadecanoyl chloride 1679-53-4, 10-Hydroxydecanoic acid 2615-15-8 5299-60-5, Ethyl 6-hydroxyhexanoate 6066-82-6, N-Hydroxysuccinimide 17696-11-6 25322-68-3, Polyethylene glycol 74124-79-1 142556-85-2 477775-62-5 RL: RCT (Reactant); RACT (Reactant or reagent) (in alkylene glycol derivs. prepn.; prepn. of insulin-alkylene glycol oligomer conjugates)			
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CN	Hexadecanoic acid (9CI) (CA INDEX NAME)			



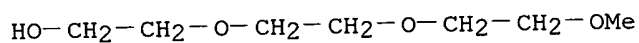
RN 75-44-5 HCAPLUS
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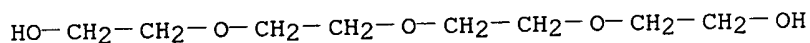
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CN Ethanol, 2-(2-methoxyethoxy)- (6CI, 8CI, 9CI) (CA INDEX NAME)



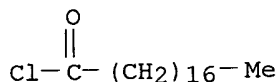
RN 112-35-6 HCAPLUS
CN Ethanol, 2-[2-(2-methoxyethoxy)ethoxy]- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



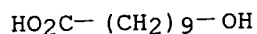
RN 112-60-7 HCAPLUS
CN Ethanol, 2,2'-[oxybis(2,1-ethanediylloxy)]bis- (9CI) (CA INDEX NAME)



RN 112-76-5 HCAPLUS
CN Octadecanoyl chloride (9CI) (CA INDEX NAME)

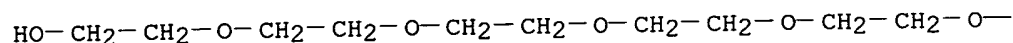


RN 1679-53-4 HCAPLUS
CN Decanoic acid, 10-hydroxy- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

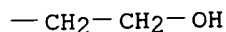


RN 2615-15-8 HCAPLUS
CN 3,6,9,12,15-Pentaoxaheptadecane-1,17-diol (9CI) (CA INDEX NAME)

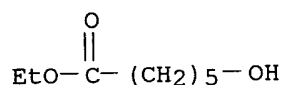
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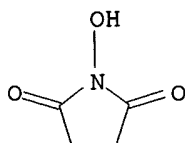
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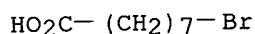
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CN Hexanoic acid, 6-hydroxy-, ethyl ester (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



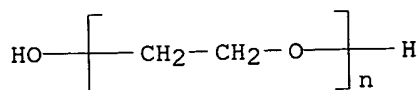
RN 6066-82-6 HCAPLUS
CN 2,5-Pyrrolidinedione, 1-hydroxy- (9CI) (CA INDEX NAME)



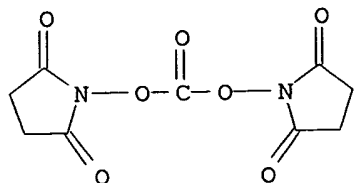
RN 17696-11-6 HCAPLUS
CN Octanoic acid, 8-bromo- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



RN 25322-68-3 HCAPLUS
CN Poly(oxy-1,2-ethanediyl), .alpha.-hydro-.omega.-hydroxy- (9CI) (CA INDEX NAME)

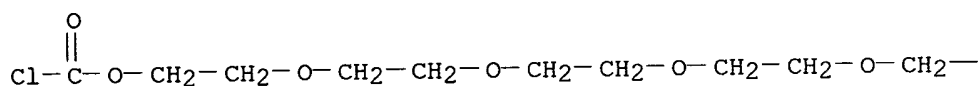


RN 74124-79-1 HCAPLUS
CN 2,5-Pyrrolidinedione, 1,1'-[carbonylbis(oxy)]bis- (9CI) (CA INDEX NAME)



RN 142556-85-2 HCAPLUS
CN Carbonochloridic acid, 3,6,9,12,15,18-hexaoxonadec-1-yl ester (9CI) (CA INDEX NAME)

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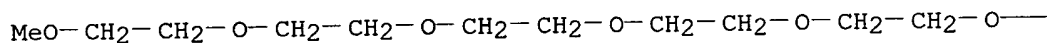


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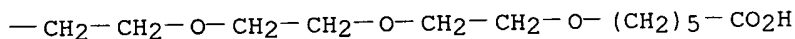


RN 477775-62-5 HCAPLUS
CN 2,5,8,11,14,17,20,23,26-Nonaoxadotriacontan-32-oic acid (9CI) (CA INDEX NAME)

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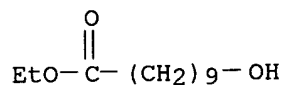
IT 3639-35-8P 4437-01-8P, 2,5,8,11,14,17,20-Heptaoadocosan-
22-ol 9004-74-4P 9004-99-3P 24342-68-5P
29823-21-0P 62304-85-2P 70802-40-3P
74654-05-0P 86259-87-2P 87117-61-1P
105292-71-5P 124668-93-5P 175172-61-9P
477775-58-9P 477775-59-0P 477775-60-3P
477775-61-4P 477775-65-8P 477775-67-0P
477775-68-1P 477775-69-2P 477775-71-6P
477775-73-8P 477775-74-9P 477775-75-0P
477781-68-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(in alkylene glycol derivs. prepn.; prepn. of insulin-alkylene glycol oligomer conjugates)

RN 3639-35-8 HCAPLUS

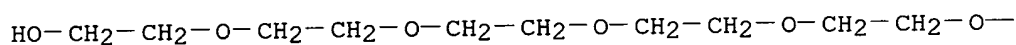
CN Decanoic acid, 10-hydroxy-, ethyl ester (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



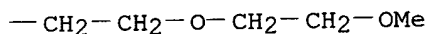
RN 4437-01-8 HCAPLUS

CN 2,5,8,11,14,17,20-Heptaoxadocosan-22-ol (6CI, 8CI, 9CI) (CA INDEX NAME)

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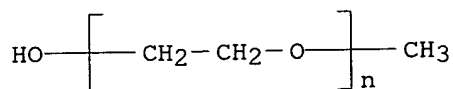


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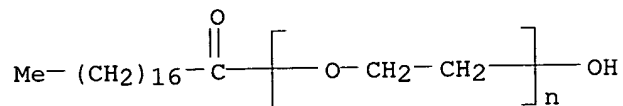
RN 9004-74-4 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), .alpha.-methyl-.omega.-hydroxy- (9CI) (CA INDEX NAME)



RN 9004-99-3 HCAPLUS

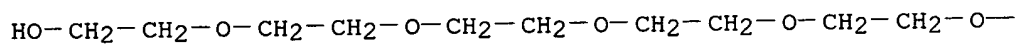
CN Poly(oxy-1,2-ethanediyl), .alpha.-(1-oxooctadecyl)-.omega.-hydroxy- (9CI) (CA INDEX NAME)



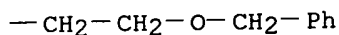
RN 24342-68-5 HCAPLUS

CN 2,5,8,11,14,17-Hexaoxanonadecan-19-ol, 1-phenyl- (9CI) (CA INDEX NAME)

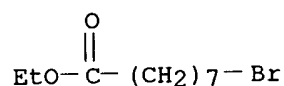
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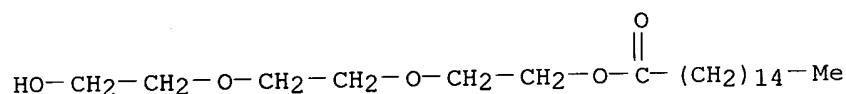
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RN 29823-21-0 HCAPLUS
CN Octanoic acid, 8-bromo-, ethyl ester (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

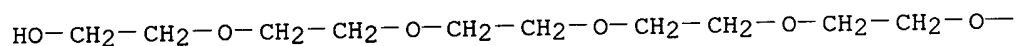


RN 62304-85-2 HCAPLUS
CN Hexadecanoic acid, 2-[2-(2-hydroxyethoxy)ethoxy]ethyl ester (9CI) (CA INDEX NAME)

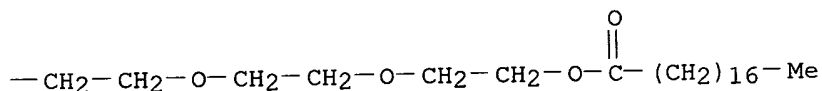


RN 70802-40-3 HCAPLUS
CN Octadecanoic acid, 23-hydroxy-3,6,9,12,15,18,21-heptaoxatricos-1-yl ester (9CI) (CA INDEX NAME)

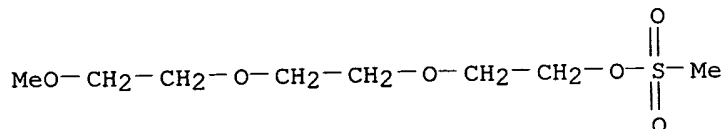
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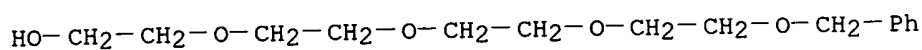
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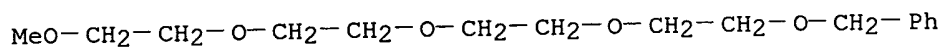
RN 74654-05-0 HCAPLUS
CN Ethanol, 2-[2-(2-methoxyethoxy)ethoxy]-, methanesulfonate (9CI) (CA INDEX NAME)



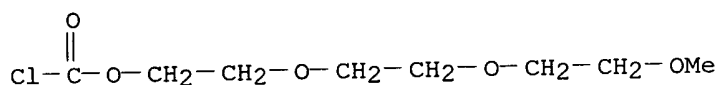
RN 86259-87-2 HCAPLUS
CN 2,5,8,11-Tetraoxatridecan-13-ol, 1-phenyl- (9CI) (CA INDEX NAME)



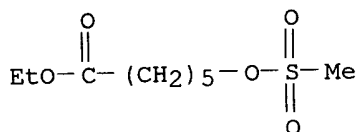
RN 87117-61-1 HCAPLUS
CN 2,5,8,11,14-Pentaoxapentadecane, 1-phenyl- (9CI) (CA INDEX NAME)



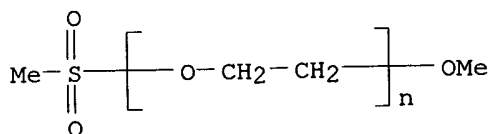
RN 105292-71-5 HCAPLUS
CN Carbonochloridic acid, 2-[2-(2-methoxyethoxy)ethoxy]ethyl ester (9CI) (CA INDEX NAME)



RN 124668-93-5 HCAPLUS
CN Hexanoic acid, 6-[(methylsulfonyl)oxy]-, ethyl ester (9CI) (CA INDEX NAME)

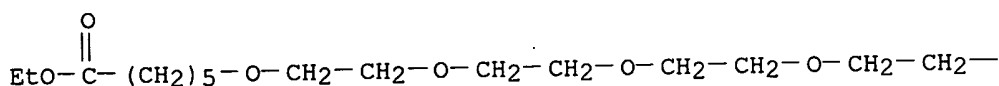


RN 175172-61-9 HCAPLUS
CN Poly(oxy-1,2-ethanediyl), .alpha.-(methylsulfonyl)-.omega.-methoxy- (9CI) (CA INDEX NAME)

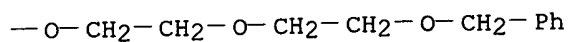


RN 477775-58-9 HCAPLUS
CN 2,5,8,11,14,17,20-Heptaoxahexacosan-26-oic acid, 1-phenyl-, ethyl ester (9CI) (CA INDEX NAME)

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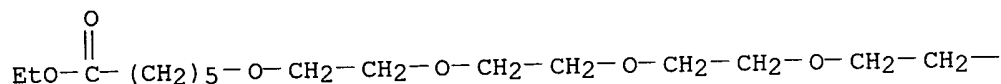


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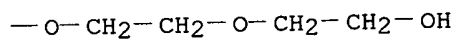


RN 477775-59-0 HCAPLUS
CN 3,6,9,12,15,18-Hexaoxatetracosan-24-oic acid, 1-hydroxy-, ethyl ester
(9CI) (CA INDEX NAME)

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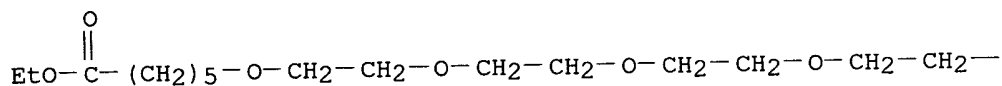


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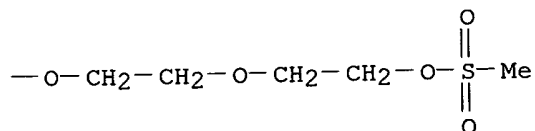


RN 477775-60-3 HCAPLUS
CN 3,6,9,12,15,18-Hexaoxatetracosan-24-oic acid, 1-[(methylsulfonyl)oxy]-,
ethyl ester (9CI) (CA INDEX NAME)

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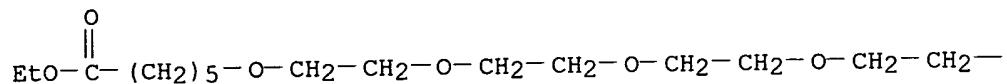


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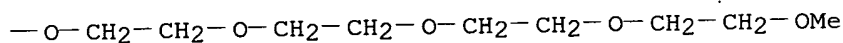


RN 477775-61-4 HCAPLUS
CN 2,5,8,11,14,17,20,23,26-Nonaoadotriacontan-32-oic acid, ethyl ester (9CI)
(CA INDEX NAME)

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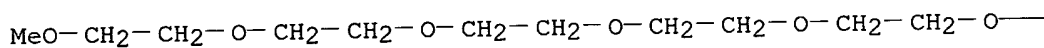


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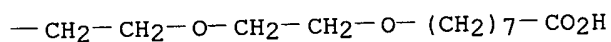


RN 477775-65-8 HCAPLUS
CN 2,5,8,11,14,17,20,23-Octaoxahentriacontan-31-oic acid (9CI) (CA INDEX NAME)

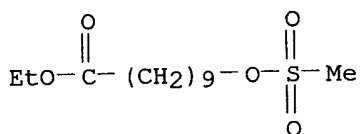
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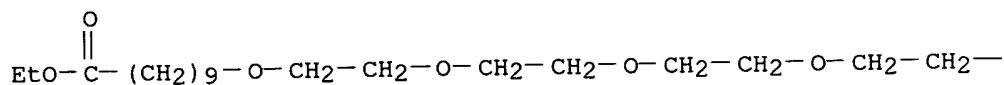


RN 477775-67-0 HCAPLUS
CN Decanoic acid, 10-[(methylsulfonyl)oxy]-, ethyl ester (9CI) (CA INDEX NAME)

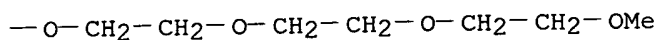


RN 477775-68-1 HCAPLUS
CN 2,5,8,11,14,17,20,23-Octaoxatritriacontan-33-oic acid, ethyl ester (9CI) (CA INDEX NAME)

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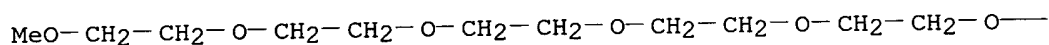


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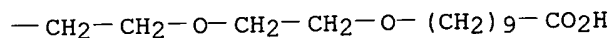


RN 477775-69-2 HCAPLUS
CN 2,5,8,11,14,17,20,23-Octaoxatritriacontan-33-oic acid (9CI) (CA INDEX NAME)

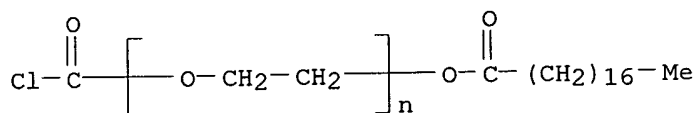
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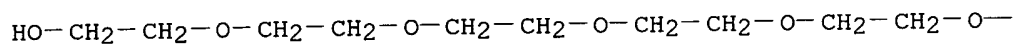


RN 477775-71-6 HCAPLUS
CN Poly(oxy-1,2-ethanediyl), .alpha.-(chlorocarbonyl)-.omega.-[(1-oxooctadecyl)oxy]- (9CI) (CA INDEX NAME)

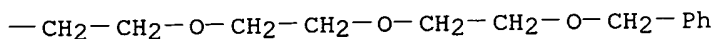


RN 477775-73-8 HCAPLUS
CN 2,5,8,11,14,17,20,23-Octaoxapentacosan-25-ol, 1-phenyl- (9CI) (CA INDEX NAME)

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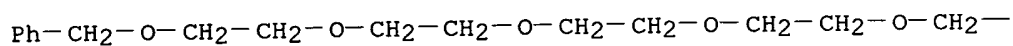


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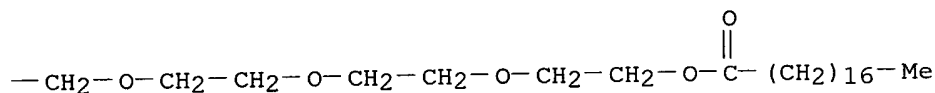


RN 477775-74-9 HCAPLUS
CN Octadecanoic acid, 25-phenyl-3,6,9,12,15,18,21,24-octaoxapentacos-1-yl ester (9CI) (CA INDEX NAME)

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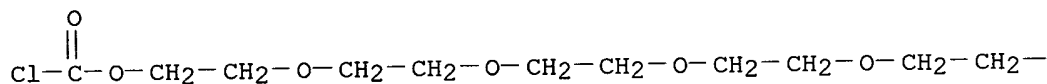


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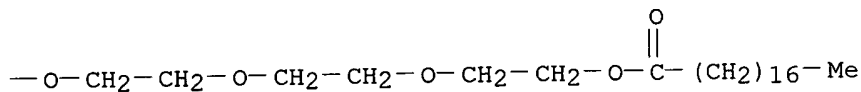


RN 477775-75-0 HCAPLUS
CN Octadecanoic acid, 25-chloro-25-oxo-3,6,9,12,15,18,21,24-octaoxapentacos-1-yl ester (9CI) (CA INDEX NAME)

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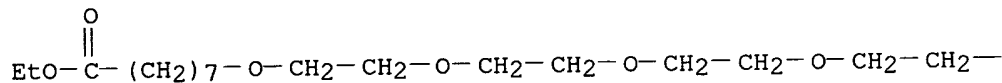


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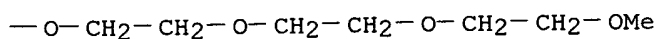


RN 477781-68-3 HCAPLUS
CN 2,5,8,11,14,17,20,23-Octaoxahentriacontan-31-oic acid, ethyl ester (9CI)
(CA INDEX NAME)

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IT 8049-62-5DP, Zinc Insulin, alkylene glycol oligomer conjugates
9004-10-8DP, Insulin, alkylene glycol oligomer conjugates

11061-68-0DP, Human insulin, alkylene glycol oligomer conjugates
 259228-98-3DP, insulin conjugates 477775-63-6DP, insulin
 conjugates 477775-66-9DP, insulin conjugates
 477775-70-5DP, insulin conjugates 477775-72-7DP, insulin
 conjugates 477775-76-1DP, insulin conjugates
 477775-77-2DP, insulin conjugates

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
 (Uses)

(prepn. of insulin-alkylene glycol oligomer conjugates)

RN 8049-62-5 HCAPLUS

CN Insulin zinc (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 9004-10-8 HCAPLUS

CN Insulin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

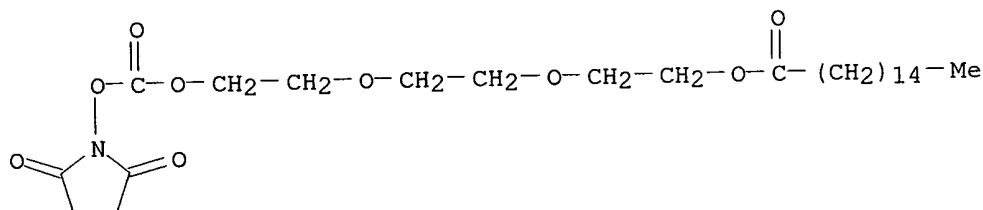
RN 11061-68-0 HCAPLUS

CN Insulin (human) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 259228-98-3 HCAPLUS

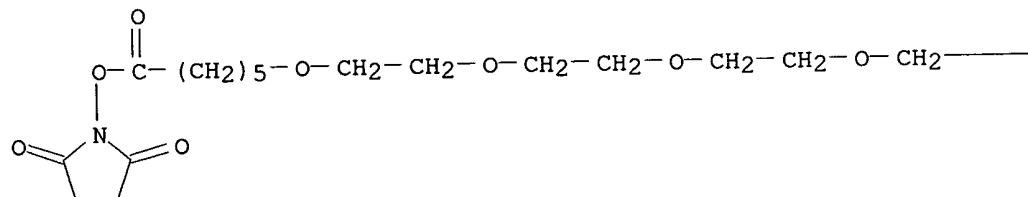
CN Hexadecanoic acid, 2-[2-[2-[[[(2,5-dioxo-1-pyrrolidinyl)oxy]carbonyl]oxy]e
 thoxy]ethoxy]ethyl ester (9CI) (CA INDEX NAME)



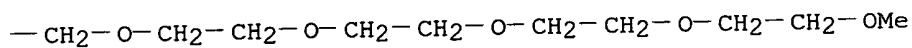
RN 477775-63-6 HCAPLUS

CN 2,5-Pyrrolidinedione, 1-[(1-oxo-7,10,13,16,19,22,25,28,31-
 nonaoxadotriacont-1-yl)oxy]- (9CI) (CA INDEX NAME)

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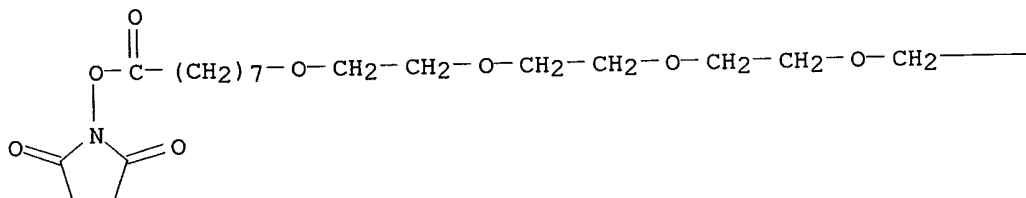


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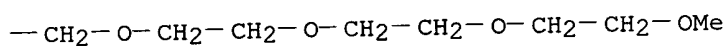


RN 477775-66-9 HCAPLUS
CN 2,5-Pyrrolidinedione, 1-[(1-oxo-9,12,15,18,21,24,27,30-octaoxahentriacont-1-yl)oxy]- (9CI) (CA INDEX NAME)

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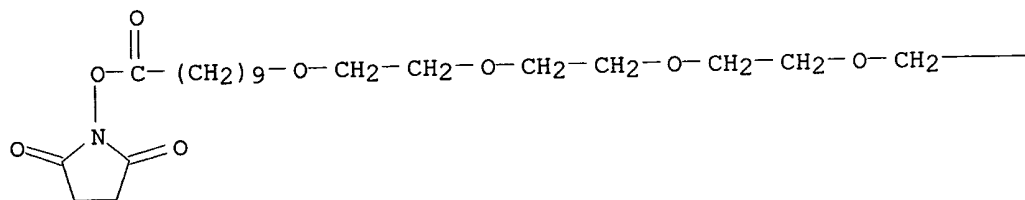


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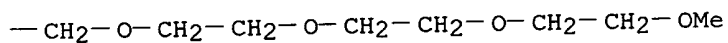


RN 477775-70-5 HCAPLUS
CN 2,5-Pyrrolidinedione, 1-[(1-oxo-11,14,17,20,23,26,29,32-octaoxatritriacont-1-yl)oxy]- (9CI) (CA INDEX NAME)

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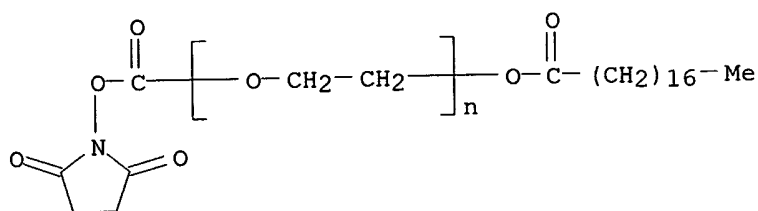


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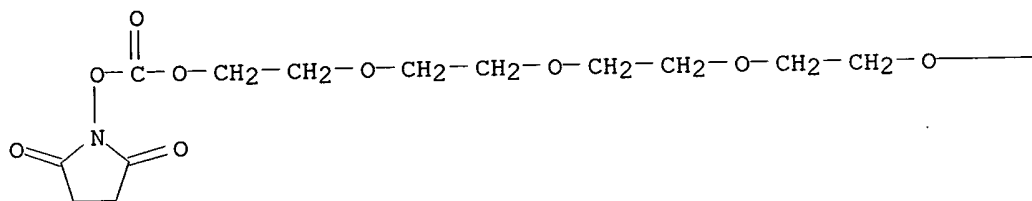
RN 477775-72-7 HCAPLUS
CN Poly(oxy-1,2-ethanediyl), .alpha.-[[(2,5-dioxo-1-

pyrrolidinyl)oxy]carbonyl]-.omega.-[(1-oxooctadecyl)oxy]- (9CI) (CA INDEX NAME)

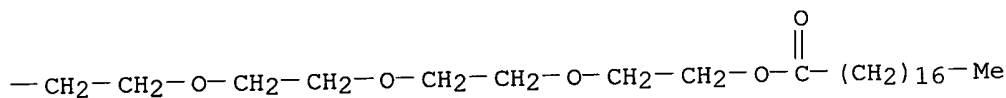


RN 477775-76-1 HCAPLUS
CN Octadecanoic acid, 25-[(2,5-dioxo-1-pyrrolidinyl)oxy]-25-oxo-3,6,9,12,15,18,21,24-octaopentacos-1-yl ester (9CI) (CA INDEX NAME)

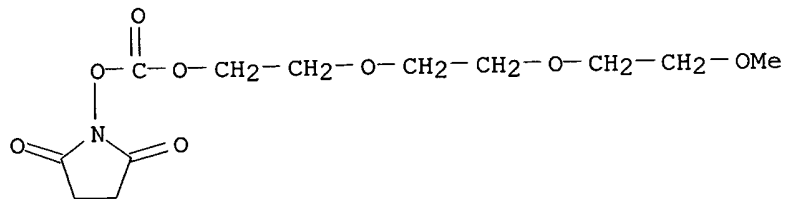
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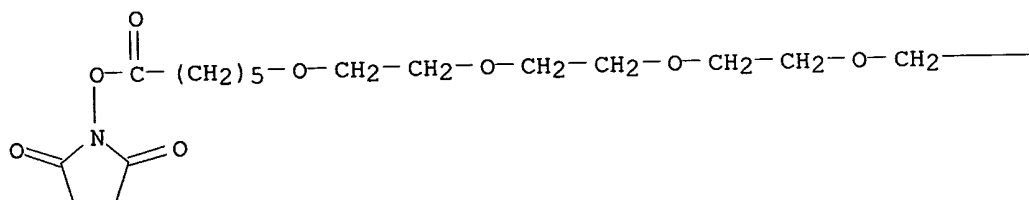


RN 477775-77-2 HCAPLUS
CN 2,5-Pyrrolidinedione, 1-[(1-oxo-2,5,8,11-tetraoxadodec-1-yl)oxy]- (9CI) (CA INDEX NAME)

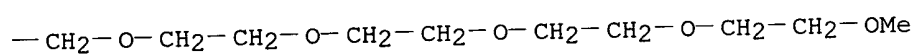


IT 477775-63-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of insulin-alkylene glycol oligomer conjugates)
RN 477775-63-6 HCAPLUS
CN 2,5-Pyrrolidinedione, 1-[(1-oxo-7,10,13,16,19,22,25,28,31-nonaodotriacont-1-yl)oxy]- (9CI) (CA INDEX NAME)

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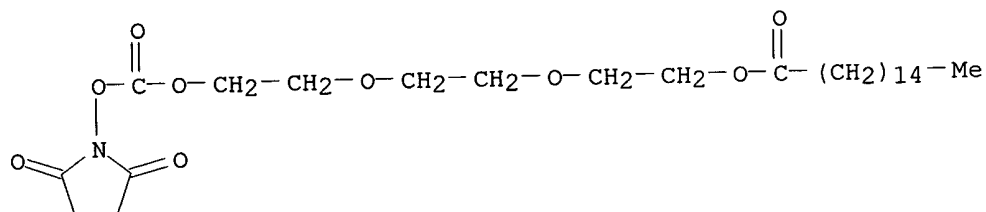


IT 259228-98-3P 477775-66-9P 477775-70-5P
477775-72-7P 477775-76-1P 477775-77-2P
477788-13-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(prepn. of insulin-alkylene glycol oligomer conjugates)

RN 259228-98-3 HCAPLUS

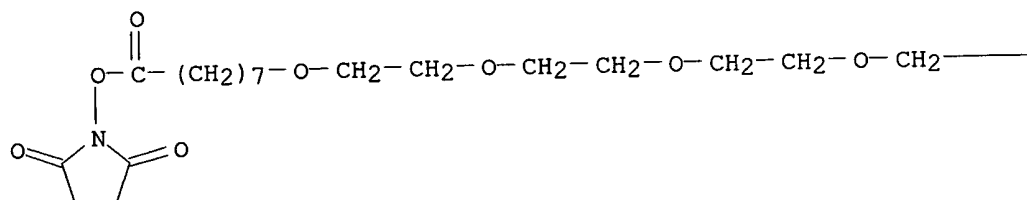
CN Hexadecanoic acid, 2-[2-[2-[[[(2,5-dioxo-1-pyrrolidinyl)oxy]carbonyl]oxy]e
thoxy]ethoxy]ethyl ester (9CI) (CA INDEX NAME)



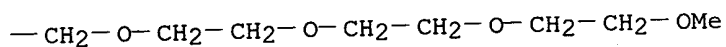
RN 477775-66-9 HCAPLUS

CN 2,5-Pyrrolidinedione, 1-[(1-oxo-9,12,15,18,21,24,27,30-octaoxahentriacont-
1-yl)oxy]- (9CI) (CA INDEX NAME)

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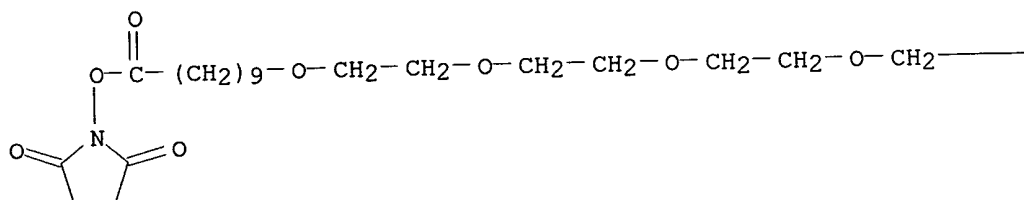


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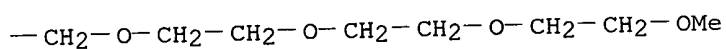


RN 477775-70-5 HCAPLUS
CN 2,5-Pyrrolidinedione, 1-[(1-oxo-11,14,17,20,23,26,29,32-octaoxatritriacont-1-yl)oxy]- (9CI) (CA INDEX NAME)

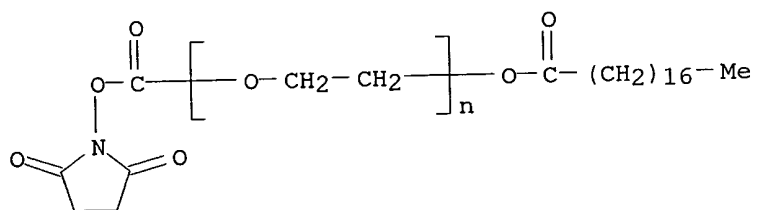
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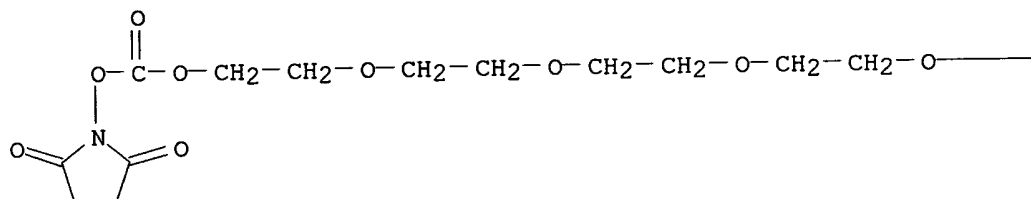


RN 477775-72-7 HCAPLUS
CN Poly(oxy-1,2-ethanediyl), .alpha.-[[(2,5-dioxo-1-pyrrolidinyl)oxy]carbonyl]-.omega.-[(1-oxooctadecyl)oxy]- (9CI) (CA INDEX NAME)

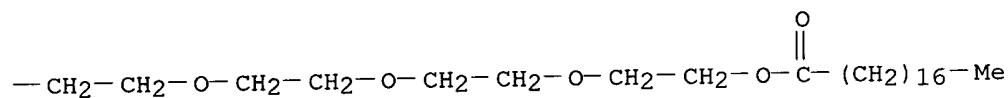


RN 477775-76-1 HCAPLUS
CN Octadecanoic acid, 25-[(2,5-dioxo-1-pyrrolidinyl)oxy]-25-oxo-3,6,9,12,15,18,21,24-octaoxapentacos-1-yl ester (9CI) (CA INDEX NAME)

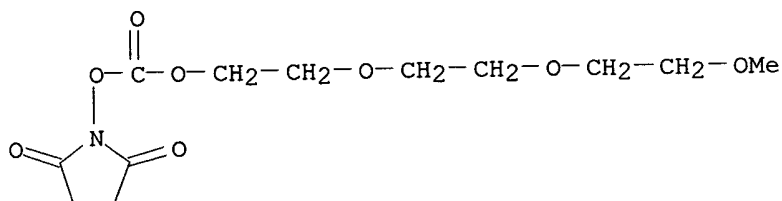
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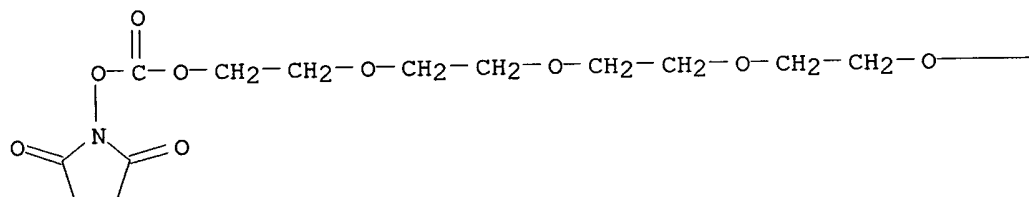


RN 477775-77-2 HCAPLUS
 CN 2,5-Pyrrolidinedione, 1-[(1-oxo-2,5,8,11-tetraoxadodec-1-yl)oxy]- (9CI)
 (CA INDEX NAME)

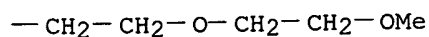


RN 477788-13-9 HCAPLUS
 CN 2,5-Pyrrolidinedione, 1-[(1-oxo-2,5,8,11,14,17,20-hepta-oxaheneicos-1-yl)oxy]- (9CI) (CA INDEX NAME)

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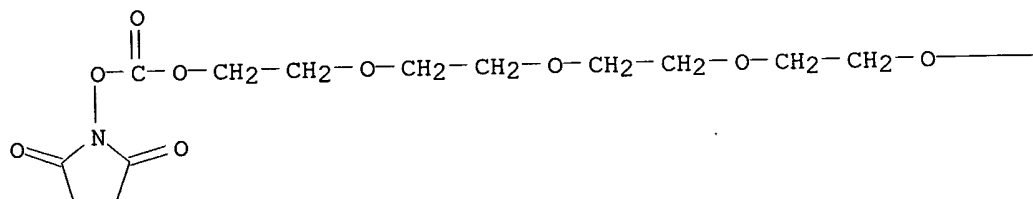


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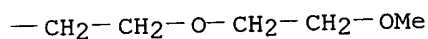


IT 477788-13-9DP, insulin conjugates
 RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (prepn. of insulin-alkylene glycol oligomer conjugates)
 RN 477788-13-9 HCAPLUS
 CN 2,5-Pyrrolidinedione, 1-[(1-oxo-2,5,8,11,14,17,20-heptaoxaheneicos-1-yl)oxy]- (9CI) (CA INDEX NAME)

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REFERENCE COUNT:

1

THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d his

(FILE 'HOME' ENTERED AT 15:30:07 ON 21 FEB 2003)

FILE 'HCAPLUS' ENTERED AT 15:32:31 ON 21 FEB 2003

E EKWURIBE NNOCHIRI/AU
L1 41 S E3-6
E PRICE CHIRSTOPHER/AU
E PRICE CHRISTOPHER H/AU
L2 19 S E3-4
E ANSARI ASLAM/AU
L3 9 S E4
E BALASINGAM RAD/AU
E BALASINGHAM RAD/AU
E ODENBAUGH AMY/AU
L4 11 S E3-5
L5 5 S L1 AND L2 AND L3 AND L4
SELECT RN L5 1-5

FILE 'REGISTRY' ENTERED AT 15:35:53 ON 21 FEB 2003

L6 129 S E1-129

FILE 'HCAPLUS' ENTERED AT 15:36:37 ON 21 FEB 2003

L7 5 S L5 AND L6

=> d cost

COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
18.81	32.29
0.54	1.20
0.00	12.66
21.60	23.45
-----	-----
40.95	69.60
2.02	2.74
-----	-----
42.97	72.34

CONNECT CHARGES

NETWORK CHARGES

SEARCH CHARGES

DISPLAY CHARGES

CAPLUS FEE (5%)

FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

CA SUBSCRIBER PRICE

IN FILE 'HCAPLUS' AT 15:42:14 ON 21 FEB 2003

=> log hold

COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
45.23	74.60

FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

CA SUBSCRIBER PRICE

SINCE FILE	TOTAL
ENTRY	SESSION
-3.26	-3.26

SESSION WILL BE HELD FOR 60 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 15:42:22 ON 21 FEB 2003